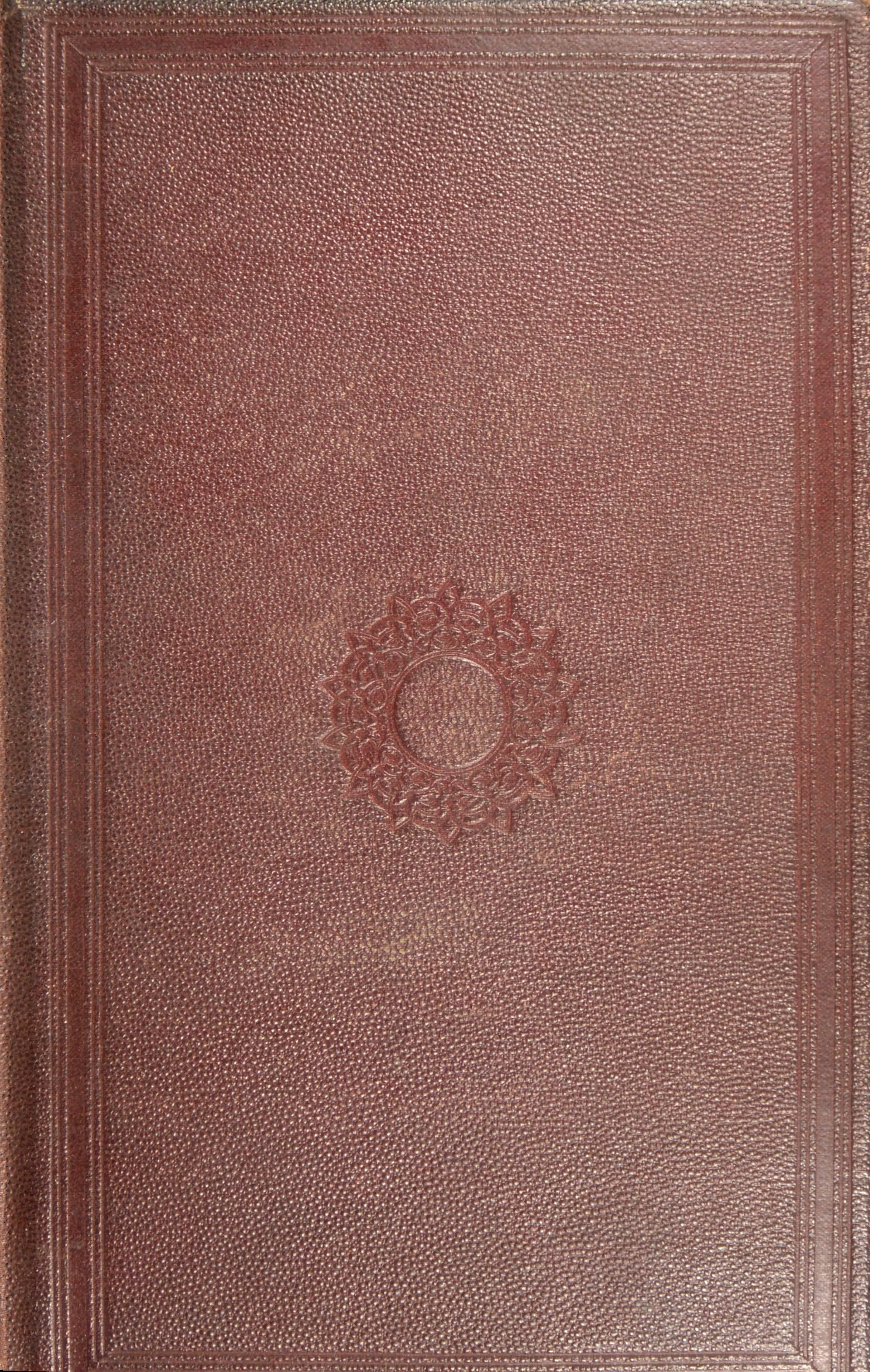

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EDITOR'S NOTE.

As the biographical sketches of the authors have not yet been received from Germany, they will be published in the next volume (probably No. XIV.).

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DISEASES

OF THE

LOCOMOTIVE APPARATUS.

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DISEASES OF THE LOCOMOTIVE APPARATUS.

In accordance with traditional usage, a certain number of disorders affecting the organs of locomotion are included in the domain of medicine. They have one feature in common, viz., that they are idiopathic, due to internal causes, or, at any rate, *not* due to a wound or external injury ; moreover, they either do not call for any operative interference, or they do so only in a subordinate degree, or for the relief of certain sequelæ. This group includes the Rheumatic Affections of the Joints and Muscles, together with some other articular and muscular disorders which are usually associated with rheumatism: gout, arthritis deformans, rickets, and mollities ossium.

The Rheumatic Affections of the Joints and Muscles (Rheumatism).

BIBLIOGRAPHY.—*Gul. Ballonius* (*Baillou*), De Rheumatismo et pleuritide dorsali, etc., in Opp. omnia IV. Genevae, 1762. p. 313.—*Sydenham*, Observationes Medicae, Sect. VI., Cap. 5 ; and Processus integri in morbis, etc., de rheumatismo.—*Cullen*, Med. pract. No. 234, etc.—*Stoll*, Rat. med. Vol. I., III., V.—*Van Swieten*, Commentar. § 1490, etc.—*Huxham*, De aëre et morbis epidemicis. London, 1752.—*Ponsard*, Traité de la Goutte et du Rhumatisme. Paris, 1770. —*Sauvages*, Nosolog. Method. Class. VII., gen. III., Rheumat.—*Chomel*, Essai sur le Rhumatisme. Paris, 1812.—*The same*, Lectures on Gout and Rheumatism, edited by Requin.—*Scudamore*, Treatise on the Nature and Cure of Rheumatism, 1816.—*Gasser*, Aperçu sur le Rhumatisme en général. Montpellier, 1817.—*Dzondi*, Die Hautschlacke oder skorischer Entzündungsreiz. Leipzig, 1822.—*The same*, Was ist Rheuma und Gicht? Halle, 1829.—*Cadet de Vaux*, De la Goutte et du Rhumatisme.—*The same*, An Infallible Remedy for Gout and

Rheumatism.—*Schönlein*, Vorlesungen über allgemeine und specielle Pathologie, etc. Würzburg, 1832. II.—*Eisenmann*, Die Krankheitsfamilie Rheuma. Erlangen, 1841.—*The same*, Die Pathologie und Therapie der Rheumatosen in genere. Würzburg, 1860.—*R. Macleod*, On Rheumatism in its various Forms.—*Todd*, Lectures on Gout and Rheumatism. London, 1843.—*Gottschalk*, Darstellung der rheumatischen Krankheiten. Köln, 1845.—*Fuller*, On Rheumatism, Rheumatic Gout, and Sciatica. London, 1860 (3d edition).—*Henle*, Rationelle Pathologie, 1853. II., p. 231.—*J. Vogel*, in Virchow's Handbuch der speciellen Pathologie und Therapie. I. 1854. p. 471.—*J. Alexander*, Rheumatism and Gout, their nature, cause, and cure. London, 1858.—*Bull*, Du rhumatisme viscéral, Thèse. Paris, 1866.—*Macario*, Mémoire sur la diathèse rhumatismale et son traitement. 1866.—*Desguins*, Du rhumatisme et de la diathèse rhumatismale. Bulletins de la Soc. de Méd. de Gand, 1868, 1869.—*Hood*, A Treatise on Gout, Rheumatism, and the Allied Affections. London, 1871.—*C. Hüter*, Klinik der Gelenkkrankheiten. Leipzig, 1871. p. 58. Also his Allgemeine Chirurgie. Leipzig, 1874, p. 220.—Consult also the various hand-books of general pathology and surgery, as well as the books enumerated in the bibliography of Gout and Rheumarthritis, and a multitude of papers contributed to the Journals.

Introductory Remarks.

The term *Rheuma* (ῥέω, I flow), like the somewhat later word *Rheumatism*, was employed by the oldest writers on medicine as a synonym of catarrh (κατὰ, ῥέω), to denote all those diseases which were attributed to the defluxion of an acrid humor, generated in the brain, into various parts of the body. It is in this sense that the words "rheuma" and "rheumatism" are repeatedly employed by Hippocrates, Galen, Paulus Aegineta, Caelius Aurelianus, Alexander of Tralles, etc. At a later period, the term "catarrh" gradually became specialized to denote affections of the mucous surfaces; while a variety of disorders, supposed to arise from the circulation of acrid humors, continued to be known as "rheumata." Ballonius was the first who definitely employed the word "rheumatism" to denote vague pains in external parts, *i. e.*, in the joints and muscles, and to distinguish them from gout, with which they had previously been confounded under the common name of "arthritis." Sydenham drew the line between gout and rheumatism more sharply still, calling the former disease "podagra." Nevertheless, long after his time, and even in the present century (Chomel, Pidoux, Alexander), we find the two affections often grouped together as divers manifestations of one and the same humoral vice—a rheumatic or gouty dyscrasia. It is only of late years that this view has been altogether abandoned.

Exposure to cold was early recognized as an undoubted cause of some, at any rate, of the affections we are now considering. Indeed, there was a tendency to assign *all* cases, for which no other cause could be discovered, to the influence of cold—a tendency fostered by the fact that the usually sudden outbreak of these painful maladies in individuals previously healthy seemed to tally better with this hypothesis than with any other. Accordingly, the causal element of chill got mixed up with the idea of rheumatism, and gradually assumed so prominent a place that the word "rheumatism" came to be almost synonymous with "disease caused by catching cold." It became usual to include under the head of "rheumatism" every painful disease in which exposure to cold could either be shown or assumed, in the absence of any other discoverable cause, to have preceded the outburst of the symptoms. The door was thus thrown open to a great variety of maladies; and towards the end of the last and the beginning of the present century, physicians had come to speak, not merely of a rheumatism of external parts—as Ballonius had done—but of a rheumatism of internal organs likewise (*rheumatismus viscerum*, *endorheumatismus*). It was not until the progress of morbid anatomy had enabled us to localize disease in the tissues and organs, and given us a deeper insight into the nature of morbid changes; not until we had discovered a multitude of previously unknown noxæ and their influence in producing structural alterations; not until the perfection of our diagnostic methods had given us power to detect disease in individual organs during life with a precision hitherto undreamt of, that the domain of rheumatism was once more restricted within reasonable limits. In the endeavor to localize disease as much as possible—to connect it with definite structural alterations—observers began to separate the disorders of internal viscera (now more easy of recognition), those of the bones, and finally the varieties of true neuralgia, from rheumatism. There still remained a group of articular and muscular affections for which morbid anatomy had failed to discover any adequate explanation, either because the comparative infrequency of a fatal issue gave little chance for post-mortem investigation, or because the changes actually found did not suffice to clear up the essential nature of the disease. For this group of maladies the term "rheumatism" has been retained up to the present time. It thus includes "all painful affections of the joints and muscles, with their tendons and fasciæ, which are either due to chill or to causes which cannot be ascertained, and are, therefore, assumed to be atmospheric."

Such a definition as this must needs cover a great variety of disorders, whose only common symptom, viz., pain (which must exist throughout the entire course, or at any rate at some stage —especially the earliest—of any disease that claims to be called "rheumatism" in the sense in which the word has hitherto been used), is very far from sufficient to serve as the distinctive mark of a pathological group. Any additional characters which may have been assigned to the group in order to justify its retention, are either wholly secondary, or else not constant, and are by no means peculiar to all the diseases which are still comprehended under the term "rheumatism." The nature of the pain—said to be exceptionally "tearing" and "dragging"—is far from being distinctive. The transient and variable character of the symptoms, the tendency to become complicated, or to alternate, with disorders of internal organs (to undergo "metastasis"),—these features are peculiar to one only of the diseases belonging to the group, viz., acute polyarthritis; they are quite foreign to those which have been described as "chronic articular rheumatism," and are wanting in a number of affections commonly known as "muscular rheumatism." Finally, the idea of a "rheumatic diathesis" is least of all peculiar to the diseases included in this group. We speak of such a diathesis when we find a patient, who has previously suffered from one or other of the above disorders, affected by it a second time or oftener; more especially if the exciting cause seems trivial, and fails to give rise to any similar disorder in other persons. But we meet with precisely the same phenomenon, *i.e.*, a tendency to repeated illness of a special kind on trifling provocation, at least as frequently in a variety of other affections, without, on that account, assuming the existence of a peculiar diathesis. We do not speak of a "catarrhal diathesis" when we find a patient getting bronchitis on the smallest occasion, or liable to repeated attacks of sore throat; still less, when a patient who has once had pleurisy is attacked by it a second, third, or fourth time, after catching cold, or even without ascertainable cause. We see no more in this than the tendency of any organ which has once suffered from disease to be affected again; or, as we often put it, to become a *locus minoris resistentiæ.* The joints, the muscles, and the parts connected with them, form no exception to the rule; they, too, are very liable to repeated attacks of any disorder from which they may have suffered once. Not even the fact—questionable as it still is—that polyarthritis is hereditary (p. 21) can be regarded as peculiar; for an inherited predisposition to disease of the mucous membranes is still more common, and undoubtedly exists in scrofula. It is certainly most inadequate to prove the existence of a "rheumatic diathesis," at least in the wide sense in which the word "rheumatism" is now employed; at the utmost, it can only prove the existence of a constitutional tendency to polyarthritis—to one only of all the diseases included in the group.

And yet the notion of a "chill" still lingers in the background; it is so intimately bound up with our idea of rheumatism as to give this nosological class the appearance of having been constructed on a substantial etiological basis. Indeed, this is the commonly accepted view; the epithet "rheumatic" is taken to mean "caused by a chill or other atmospheric influence," and the word "rheumatism" is specially applied to those articular and muscular affections which are due to a chill or other atmospheric cause, and which are therefore understood to be of a "rheumatic" nature. Nevertheless, this view is unmistakably defective. First, as regards the phenomenon of "chill" itself. This is far from being purely imaginary, as many people are nowadays inclined to think; on the contrary, it would be the part of wilful blindness to deny its existence; but it is likewise true that the term is far from definite, and

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that the mechanism of the process is highly obscure. It is constantly being misapplied both by the profession and by the public to denote every sort of noxa, known and unknown, and often as a cloak for ignorance of the true morbific agency. But even if we restrict the term "chill" to its primary etymological meaning, viz., a hurtful withdrawal of heat, we shall still find it impossible to maintain the above conception of "rheumatism," for the maladies included in it are by no means always due to a demonstrable chill; on the contrary, many of them are certainly due to causes of an entirely different kind (*e. g.*, *Myalgia cervicalis*, *lumbalis*). These, at any rate, would have to be eliminated, if we desired to construct a pathological group on the etiological basis of "chill." But even this would not dispose of all our difficulties. There would be no reason for limiting the term "rheumatism" to the joints and muscles—no reason why we should not return to its older denotation, which had, at any rate, the merit of logical consistency, since it comprised *all* diseases known or believed to be caused by chill, the subdivisions of the group being founded on the particular organ affected (rheumatism of the brain, lungs, pleura, joints, etc.). After all, the joints and muscles exhibit no exclusive or even pre-eminent susceptibility to the effects of the chill; the respiratory organs, for example, are on a level with them, or perhaps above them, in this respect. Moreover, even those muscular and articular affections which are really due to chill, are not thereby individualized and marked off from their neighbors; on the contrary, they occur under many forms, any of which may result from other noxæ, as readily as from this. The truth is —and here we have the final and conclusive objection to the scheme—that chill, whatever meaning we may put upon the word, is quite incompetent to serve as a *fundamentum divisionis* in nosology. Chill as a morbific agent presents no analogy to a poison which, when it has once entered the body, invariably gives rise, under similar conditions, to a train of similar phenomena of a kind peculiar to itself; no, it represents, for the most part, an aggregate of processes which operate as so many distinct attacks upon any and every organ and tissue in the body, and which may therefore lead to an endless variety of consequences.

As regards "other atmospheric influences," their relation to the diseases we are now considering is either hypothetical or so obscure as to render them all but synonymous with "unknown influences." Hence, they are even less suited than "chill" itself to serve as a basis for nosological classification.

We are thus landed in the conclusion that the group of diseases included under the head of "rheumatism," taking the word in its usual sense, has no *raison d'être* from the point of view either of morbid anatomy or of etiology; neither does it represent any constant aggregate of clinical symptoms. The word itself is a survival from a time when medicine did not aspire to anything beyond a merely symptomatic conception of the majority of diseases. Where knowledge of the intimate phenomena ran short, the gap was stopped with speculative and hypothetical assumptions. Thus the fundamental link between the diseases denoted by the term "rheumatism," and grouped together in virtue of purely superficial characters, was looked for—now in a rheumatic poison or acid crasis, now in electrical conditions of an abnormal kind,—nay, even in a similarity of reaction to particular remedies, etc. These hypotheses have all broken down, at any rate in their application to the diseases collectively designated "rheumatism." Every attempt to bring the latter under a common category, with a claim to scientific recognition, has failed in the past, and will probably fail in the future. For "rheumatism," as now understood, possesses as little pathological homogeneity as it did at a former period, when its domain was wider than it now is. Its limits have been gradually narrowed, year by year; gout, arthritis deformans, the articular neuroses and other forms of neuralgia, the painful affections of the muscles depending on toxic and infective processes, have been successively withdrawn, as they were found to be disorders *sui generis*, or due to special causes. We may fairly anticipate that the pathological residue which is still comprised under the head of "rheumatism" will continue to undergo the same process of differentiation, for there can be no doubt that it includes diseases which are radically heterogeneous. For instance, "acute articular rheumatism" and "chronic articular rheumatism" have only the most superficial resemblance to each other. They both affect the joints, and that is the sole feature they have in common; in all other respects they are profoundly unlike. One is acute, the other chronic; but this is the least important of their differences. The former is an acute febrile constitutional disease, pathologically allied to other acute constitutional diseases, more especially to certain infective maladies[1] (malarial fever, influenza), while the latter is a purely local affection, whose relation to the former may fairly be likened to that which subsists between a bronchial or conjunctival catarrh and an attack of measles. (Cf. Chronic Rheumatic Arthritis.) Then again, "gonorrhœal rheumatism," by virtue of its causal connection with urethral inflammation, is so thoroughly distinct both from this and from every other form of rheumatism, that its etiology alone is enough to exclude it from a group of diseases attributed to "chill or other atmospheric influences." Finally, "muscular rheumatism" forms a wholly indefinite category, which comprises all painful affections in and about the muscles to which no other berth can be assigned. We may be allowed to say of it, in the words of the old rule: "Pains which do not admit of being defined are termed rheumatism."

Accordingly, if "rheumatism" cannot be maintained as a nosological category, it necessarily follows that the term itself is not merely superfluous, but, as has been pointed out by Henle, and more recently by Hueter, positively detrimental; since it calls up erroneous, or, at any rate, unfounded notions of an underlying harmony between various forms of disease, some of which we know to be distinct, while concerning others we are very ignorant. These objections, however, do not apply to the adjective "rheumatic." This is used, in a general way, to denote affections caused either by an actual chill, *i. e.*, a hurtful withdrawal of heat from the body, or, by some unknown agency, concerning which we know or are able to assume that it is not of a coarsely mechanical kind, nor yet a poison or contagion, and which we therefore suppose to be a physical change in the atmosphere. We are justified in keeping the term "rheumatic" in this sense—in which alone it is now employed—for the sake of convenience. It involves no theory. Its rejection would oblige us to enumerate all the above-named causes in every instance, specifying them as present or absent. Moreover, the effects of a chill are frequently combined with those of other atmospheric conditions, without our being able to unravel the combination or to assign each part of the complex result to its appropriate cause.

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[1] Cf. *Hirsch*, Handbuch der historisch-geographischen Pathologie, I., p. 598.

I have already explained, at some length, that even the admission of a common "rheumatic" cause for diseases otherwise unlike does not entitle us to throw them into a single group. Accordingly, we are not inconsistent in discarding both the name and the group "Rheumatism," while we retain the epithet "rheumatic," at any rate until the various causal factors still embraced under the latter term have come to be fully understood. On the contrary, we simply obey the usual custom in pathological nomenclature, and keep within the present limits of our knowledge, when we distinguish those diseases whose morbid anatomy has been thoroughly investigated (the articular class) as *arthritis*, *arthromeningitis*, or *polyarthritis*, according to the parts chiefly or exclusively involved; while we designate the muscular affections, about whose anatomy we know less, broadly as *myopathies*—or, since pain is the leading feature in most of them, as *myalgias;* both the articular and the muscular class of these affections being termed "rheumatic," in order to distinguish them from symptoms or structural alterations of a similar kind arising from other causes.[1] The addition of the epithet "rheumatic" does not involve any closer relationship between these two kinds of process than may be supposed to exist between a "rheumatic" pleurisy and a "rheumatic" paralysis; neither does it imply any theory as to the local or constitutional nature of any given malady.

In harmony with the above principles, the following are the diseases to be described in the ensuing pages: first, *Rheumatic*

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[1] The anatomical nomenclature of "rheumatic" joint-affections proposed by Hueter is inadequate for the purpose in view. For instance, the term "Polyarthritis synovialis," for acute rheumatic polyarthritis, is not enough to distinguish it from other forms of multiple synovitis, such as the pyæmic, and many others which have not yet attracted much attention (*e. g.*, the scorbutic form).

Polyarthritis or *Rheumarthritis*, essentially a constitutional disease ; next, those affections which may be regarded as of local nature, viz., *Chronic Rheumatic Arthritis* and the various forms of *Rheumatic Myopathy* or *Myalgia.* As a disease of the joints, *Gonorrhœal Arthromeningitis* is included among the disorders of the locomotive apparatus, while with the "rheumatic" forms of myopathy we associate certain other affections of the muscular system usually dealt with by the physician.

1. Polyarthritis rheumatica acuta.

Special Bibliography.—*Haygarth*, A Clinical History of Acute Rheumatism. London, 1806.—*Davis*, Untersuchungen über Herzentzündungen nebst *Wells*' Bemerkungen über Rheumatismus des Herzens. Deutsch. Halle. 1816.—*Bouillaud*, Nouvelles recherches sur le rhumatisme articulaire. Paris, 1836.—*The same*, Traité du rhumatisme aigu. Paris, 1840.—*Furnivall*, On the Pathology of acute rheumatism and the prevention of heart-disease. Lancet, 1844. I. 11. —*Kubik*, Beiträge zur Therapie des Rheumatismus. Prager Vierteljahrschrift. 1847. XV. p. 124.—*Dechilly*, Bulletin de l'Acad. de Méd. 1850, p. 665.—*Kersten*, Beiträge zur Beh. des hitzigen Gelenkrheum. Deutsche Klinik, 1849. 26.—*Bouchardat*, Sur la pathogénie et la thérapeutique du rhumatisme art. aigu. Annuaire de Thérapeutique. 1851.—*Gurlt*, Beiträge zur vergleichend. pathol. Anat. der Gelenkkrankheiten. Berlin, 1853.—*Wunderlich*, Handbuch der spec. Path. u. Therap. 1856. p. 612.—*Hegner*, Der acute Gelenkrheumatismus u. seine Behandlung durch Citronensaft. Dissert. Zürich, 1857.—*Gubler*, Sur le rhumatisme cérébral. Arch. gén. de Médecine, 1857. I. 264.—*Lebert*, Klinik des acuten Gelenkrheumatismus. Erlangen, 1860.—*Griesinger*, Ueber die protrahirte Form der rheumat. Hirnaffection. Archiv d. Heilkunde, 1850. I. p. 235.—*Tüngel*, Klinische Mittheilungen. Hamburg, 1862. p. 102.—*Rauchfuss*, Ueber Gelenkentzündung u. s. w. im Säuglingsalter. Petersburg. mediz. Ztschrift. 1863. IV. p. 193.—*Chambers*, British Med. Journal, 1863. No. 139. —*R. Volkmann*, in Pitha u. Billroth's Hdb. der Chirurgie. II. 1865. p. 491.—*H. Davies*, On the treatment of rheumatic fever in its acute stage exclusively by free blistering. London, 1864.—*The same*, London Hospital Reports, 1866. II. 138.—*Fervet*, Du rhumatisme artic. et de son traitement par les vésicatoires. Arch. géner. 1865. II. 531.—*Th. Simon*, Ueber Geisteskrankheiten im Verlauf des acuten Gelenkrheumat. Annalen des Charité-Krankenhauses. XIII. 1865. p. 67. —*Vernay*, Gaz. méd. de Lyon, 1867. No. 2–5.—*Fuller*, Guy's Hosp. Reports, 1867. 1.—*The same*, On the nature of rheumatic inflammation, etc. Brit. Med. Journal, 11 April, 1868.—*Gull & Sutton*, Remarks on the natural history of

rheumatic fever. Med. Chir. Trans. 1869. II. p. 43.—*H. Ferber*, Die nervösen Erscheinungen im Rheum. acutus. Archiv. d. Heilk. 1869. X. 253.—*The same*, Rheumatismus, Chorea, Herzaffection. Ibidem. 1871. XII. 1.— *W. H. Dickinson*, Tables illustrating the effect of remedies, etc. Lancet, 1869. I. No. 5-8.—*C. Hüter*, Klinik der Gelenkkrankheiten. Leipzig, 1871. pp. 58-203.—*C. Heymann*, Ueber Rheumatismus. Virchow's Archiv. 1872. LVI. Heft 3.—*Aug. Mayer*, Ueber die complicationen des acuten Gelenkrheumat. Diss. Berlin, 1872.—*L. Concato*, Il rheumatismo articolare acuto e l'apparechio inamovibile. Rivista Clinica. 1869, No. 1, and 1872, No. 27.—*Picot*, Du rhumatisme aigu, etc. Paris, 1873.— *W. Winternitz*, Ueber Katarrhalische u. rheumatische Processe und ihre Behandlung. Mittheil. des ärztlich. Vereins in Wien, 1873. No. 22.—*Runge*, Die Erkältung. Deutsch. Archiv für klin. Mediz. XII. 220.—*Oehme*, Die Behandlung des Rheum. acutus mit festen Verbänden. Archiv der Heilk. XIV. 385.—*Gueneau de Mussy*, Leçons cliniques sur le traitement du rhumatisme. Union Médicale. 1873. 3-17.—*F. Hartmann*, Der acute und chronische Gelenkrheumatismus. Erlangen, 1874.—*F. Falk*, Ueber Entstehung von Erkältungskrankheiten. Reichert. u. Dubois-Reymond's Archiv. 1874. p. 159.

Acute rheumatic polyarthritis [*rheumarthritis*, *polyarthritis synovialis* (Hueter), *febrile rheumatism of the joints*] is a constitutional, non-infecting malady, attended by fever, which sets in with inflammation of and exudation into the joints, and often with inflammation of internal organs also, especially of the serous membranes.

I have already stated in the course of my introductory remarks that the physicians of antiquity and of the middle ages were well acquainted with this disease, although they confounded it with other affections of the joints, under the general name of "arthritis." Even in Hippocrates (*De Affectionibus.* Ed. Kühn, Lipsiae, 1825, II., 406) we find mention made of a form of arthritis, attended with fever, during which now one, now another joint becomes painful, occurring by preference in the young, seldom proving fatal,—a description which can only apply to rheumarthritis. Later writers added little to this account of the disease; they preferred to discuss its essential nature by the light of the pathological doctrines of their day, and tried to elucidate the shifting character of the joint-symptoms and the frequent occurrence of visceral complications—the latter a fact which had also been known from of old. Cullen was the first to take a decided step in advance, by laying stress on the inflammatory character of the joint-affection, and by separating it, not only from gout (as some of his predecessors had already done), but also from chronic rheumatic arthritis (so-called "chronic articular rheumatism"), and from rheumatic affections of the muscles (muscular rheumatism). A still more important addition was made to our knowledge when diligence in post-mortem investigation disclosed the special frequency of cardiac mischief—pericarditis, endocarditis, myocarditis. Wells seems to have been the first to point out the connection of these disorders with polyarthritis, and actually to designate them as "rheumatism of the heart." When, during the early part of this century, we became better able to recognize the existence of such complications during life, observations rapidly accumulated, especially in France, showing the frequency of inflammation of the heart and of other organs in the course of rheumarthritis (*e. g.*, Chomel, loc. cit., and in Dictionnaire de Médecine, article Pericarditis, etc.; Andral, Clinique Médicale, 1835, II., 502; III., 416). It was Bouillaud, more particularly, who drew general attention to the cardiac complications of acute rheumarthritis. He went too far, however, in viewing them as normal features of the disease.

French physicians, again (Hervez de Chégoin [1845], Gubler, et al.), were the first to give special attention to the occurrence of severe cerebral symptoms in certain unfavorable cases of this disease. Within the last ten years, moreover, a rapid elevation of temperature has been observed to precede the fatal issue in most cases of this kind.

Finally, Griesinger was the first to notice the relation of certain forms of insanity to a previous attack of rheumatic polyarthritis. He believed them to be essentially connected with the rheumatic process.

Etiology and Pathogeny.

We are acquainted with a variety of conditions, some general, others special, which favor the development of rheumarthritis. Among the former, climate and season occupy a foremost place. According to Hirsch (l. c.), "rheumatic fever, in marked contrast to the other disorders usually included under the head of rheumatism, and which are all but universally distributed over the earth's surface, must be regarded as pre-eminently a disease of temperate latitudes." It is rarely met with in the polar regions, while our information about its prevalence in hot countries is very contradictory. This may be ascribed partly to telluric differences, partly to differences of race—the liability of the inhabitants of a given country varying as they happen to be indigenous or immigrant,—partly, no doubt, to the inadequate data at our disposal, and the variable denotation of the term "rheumatism"; but even in temperate regions, more especially in northern and central Europe, the distribution of the disease is highly irregular. In many parts, indeed, as in Cornwall, Guernsey, and the Isle of Wight, in the Belgian Canton of Beauraing, in Jekaterinoslaw, the disease appears to be either unknown or excessively rare (Hirsch, loc. cit.). So, too, the ratio between the frequency of acute articular rheumatism and that of other diseases is far from being a constant one.

The data now at our disposal show that the proportion of cases of acute rheumatism to the sum total of disease may vary (in Europe) from 1.2 per cent. (Stuttgart) to 11.5 per cent. (London).

As regards the influence of the seasons, in our temperate climate, all comparisons extending over a sufficiently large series of observations agree, notwithstanding minor discrepancies, in assigning the maximum prevalence of the disease to the inclement part of the year (from October to May), while there is a falling-off during the summer months (July, August, September).

At Zurich, according to Lebert, during the years from 1853 to 1859, out of 220 cases 27.4 per cent. occurred from January to March, 31.8 from April to June, 20.2 from July to September, 20.6 from October to December. The highest percentage was reached in April (13.3 per cent.) and January (9.5 per cent.). At Würzburg, Roth[1] found that out of 79 patients seen from 1857–1860, 30.2 per cent. came under treatment during the first quarter of the year, 36.5 per cent. during the second quarter, 16.3 per cent. during the third, 27.7 per cent. during the fourth.

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[1] Verhandlung der Würzburg. phys. med. Gesellschaft 1863, iv. 277.

Fiedler's[1] statistics, taken from the Dresden hospital, show 27.19 per cent. for the first quarter, 27.34 per cent. for the second, 16.74 per cent. for the third, 28.73 per cent. for the fourth. At Munich, Huber[2] found, for 1865–66, that out of 90 cases 27 belonged to the first quarter, 24 to the second, 10 to the third, 29 to the fourth. At Copenhagen, Lange,[3] taking the period from 1842 to 1865, found the maximum number of cases to occur in January, the minimum number in September. Wunderlich gives the following figures for the four quarters of the year:[4] first quarter, 30.3 per cent.; second, 23.5 per cent.; third, 17.9 per cent.; fourth, 28.08 per cent. At the Rudolfsspital in Vienna the maximum number of cases, admitted for "acute rheumatism" in 1871, occurred in February, December, January, March; in 1872, in December, February, March, June, and January; the minimum in both years occurred from July to September. At Berlin, according to statistics including a large number of patients in all ranks of society,[5] the figures for acute rheumatism stood as follows: in 1867, first quarter, 182; second quarter, 112; third, 50; fourth, 106. In 1868, first quarter, 123; second, 60; third, 57; fourth, 86. In 1869, first quarter, 76; second, 124; third, 44; fourth, 74.

In certain years the disease is so unusually prevalent in a particular country as to assume the character of an epidemic. Some of the older writers on medicine (Lange, Pringle, Lancisi, Stoll, Mertens, Stoerck) actually speak of "epidemics of rheumatism," though the essential feature of an epidemic disease—infective power—is wanting to rheumarthritis. It is probable that atmospheric influences may contribute to this occasional increase of frequency, but we have no trustworthy data on the subject.

According to Lebert, the year 1857, at Zürich, was remarkable for the number of cases of rheumarthritis that occurred. The disease was specially prevalent at Dresden in 1857 and 1862 (Fiedler), at Copenhagen in 1844–46, 1849, 1852, 1857–60, 1862–64 (Lange).

Among the special predisposing causes of rheumarthritis, occupation and mode of life stand foremost. Persons exposed by the nature of their calling to frequent and extreme changes of temperature, or insufficiently protected against sudden chills during active bodily exertion, are specially liable to the disease. Next in order of hurtfulness stands residence in damp rooms, especially sleeping in a damp house; but this appears to be less prone to cause acute polyarthritis than the chronic forms of articular inflammation and so-called muscular rheumatism.

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[1] Archiv d. Heilkunde. 1866, VII. 156. 1874, XV. 154.

[2] Bayer. ärztlich. Intelligenzblatt. 1867, No. 46.

[3] Studien over den acute Ledderrheumatisme. *Virchow* and *Hirsch's* Jahresbericht, 1866. II. 269.

[4] Speciell. Pathol. u. Therapie, 1856, 612.

[5] Beilagen zum Communalblatt der Stadt Berlin. These reports are unfortunately untrustworthy in other respects, owing to the want of uniformity in the returns furnished by different practitioners. They ceased to appear when the war broke out in 1870.

Of 76 patients admitted into the Paris Charité, Chomel found the majority to be cabmen, day-laborers, shoemakers, and bakers. Lebert states that out of 121 patients at Zurich, whose occupation was specified, 85 followed callings which exposed them to the influences enumerated above. Fiedler noticed a preponderance of smiths, bakers, laborers, and maid-servants among his cases; of the entire number of patients following these occupations 7.1–11.3 per cent. suffered from polyarthritis; while only 2.3–2.6 per cent. of the tailors and shoemakers admitted into the wards, and of tradespeople, etc., a still smaller proportion, suffered from this disease. Of fifty-six cases observed by myself (none of them in a hospital), the majority occurred in coachmen, railway artificers, smiths, artisans (both male and female), and cooks.

Age is an important factor in the causation of rheumarthritis. Youth and early manhood are especially liable to the disease, the favorite period lying between puberty and the age of thirty, that from the thirtieth to the fiftieth year coming next in order. After fifty, first attacks are extremely rare; subsequent ones are less uncommon. Children under four are scarcely ever affected; the disease becomes progressively more common after the fifth year, obviously because the development of muscular activity, out-door pursuits, going to school, etc., furnish more opportunities of exposure to the injurious influences alluded to above.

It is hardly possible to find a clear instance of a first attack of rheumarthritis after the age of sixty, in medical literature. On the other hand, we occasionally come across instances, especially in the older authors, of "acute articular rheumatism" occurring in infants just after birth, or still at the breast; the majority of these records are probably to be attributed to errors of diagnosis, pyæmic or syphilitic diseases of the bones or joints having been mistaken for rheumarthritis.

Rauchfuss met with only two cases of polyarthritis among 15,000 infants at the breast during a period of four years. Widerhofer[1] observed the disease in a baby twenty-three days old, in the Foundling Hospital at Vienna,—the only case of the kind that occurred among 70,000 children in eight years. Stäger[1] met with it in a baby four weeks old; another case recorded by him is, to say the least of it, doubtful; and the same uncertainty clings to two out of three cases reported by Bouchut.[2] Henoch[3] has put a case of rheumarthritis in a child ten months old on record; Roger[4] has published one case in a child of two, another in one of three years.

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[1] Jahrbuch für Kinderkrankheiten. 1859. 157.

Sex does not appear to influence the frequency of the disease, except in so far as one or other of the occupations which predispose to this disease happens to be chiefly followed by men or by women.

Among 230 patients Lebert found 119 males and 111 females. Wunderlich had 65 males to 43 females; Roth 38 males to 41 females; Fiedler 281 males to 370 females (in the year 1873, 61 males to 64 females); Kreuser,[5] in Stuttgart, 44 males to 43 females; Huber 49 males to 41 females. In the Rudolfsspital at Vienna, in 1871, they had 75 males to 45 females; in 1872, 62 males to 46 females, admitted with "acute rheumatism." Among my own 56 patients I had 27 males to 29 females; and out of 1,370 patients at Berlin, from August, 1866, to September, 1870, 678 were males, 692 females.

A former attack renders a patient peculiarly liable to others; and this liability is often increased by subsequent attacks, the intervals between successive illnesses becoming progressively shorter, while the illnesses themselves last longer, and the local disturbances become more severe and ultimately lapse into a chronic state. The first attack is usually separated from the second by an interval of from three to five, sometimes even of ten years. Nevertheless, the number of persons who have actually suffered from more than one or two attacks of rheumarthritis is relatively small. For, when the disease shows itself in early life, it is prone to be complicated with cardiac mischief, to which the patient soon succumbs; while, as I have already mentioned, the tendency to the disease is diminished with advancing years.

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[1] Journal für Kinderkrankh. 1856. VI.

[2] Diseases of Children. Transl. by P. H. Bird, 1855, p. 706.

[3] Beiträge zur Kinderheilkund. N. F. 1868.

[4] Archives générales. 1867. I., p. 54.

[5] Würtemberg. Correspondenz-Blatt. 1866. No. 2.

Of Lebert's 53 patients, 27 had suffered from one previous attack, 8 from two, 4 from three, 6 from four, 4 from five, and 4 from a still greater number.

Again, there are certain diseases during or after which polyarthritis is exceptionally prone to occur; I allude chiefly to scarlet fever and dysentery. The liability of the patients to articular complications varies in different epidemics of these two diseases; but this may possibly be due—apart from any *genius epidemicus*—to the state of the weather and other circumstances of a local order. When polyarthritis occurs in connection with scarlet fever, it usually sets in during the period of desquamation; when in connection with dysentery, on the other hand, it comes on after the patient has quite recovered and has resumed his usual occupation, suffering at most only from a certain degree of weakness. We know nothing certain about the nature of the connection between rheumarthritis and these antecedent maladies. If we choose to indulge in speculation on the subject, we may suggest that the skin, whose state may undoubtedly contribute to the development of polyarthritis, has been rendered more sensitive, more liable to be affected by the exciting causes of the disease, in consequence of its previous hyperæmia and the removal of its cuticular layers.

Again, the puerperal state appears to act as a predisposing cause of rheumarthritis. Its possible influence may have been exaggerated in former days, when pyæmic arthritis, which not unfrequently occurs in connection with puerperal fever, was not distinguished from other inflammatory affections of the joints. So far as my own observations enable me to judge, those women who have lost much blood during labor are especially liable to the disease; indeed, it is by no means rare as a consequence of abortion. It may be that here also the hyperæmia of the skin which occurs during labor, and with which the abundant sweating is associated, may be connected with the articular affection, while the loss of blood and other discharges operate only by reducing the power of the organism to make head against hostile influences of whatever kind.

It is quite possible that, under special climatic conditions, other febrile maladies may likewise predispose the system to become affected by rheumarthritis. Thus Duffey[1] asserts that it not unfrequently occurs in Malta, during convalescence from certain typhoid forms of fever endemic in that island.

Again, Volkmann[2] has seen polyarticular arthritis setting in with acute fever, and as rapidly subsiding, during the invasion stage of syphilis. But these symptoms are probably due to the specific infection (*Cf.* Vol. III., p. 177). Finally, gonorrhœa is usually numbered among the predisposing causes of rheumarthritis; but the articular inflammation which is occasionally associated with gonorrhœa is essentially distinct from rheumarthritis, and ought not to be confounded with it. (*See* Appendix: *Arthromeningitis gonorrhoica*).

Pidoux and Graves appear to have been the first to call attention to the occurrence of rheumarthritis after scarlet fever. They were followed by Murray, Chomel-Grisolle,[3] and Valleix; but their discovery was forgotten until it was resuscitated by Trousseau.[4]

The connection between rheumarthritis and dysentery may possibly have been known to the oldest writers on medicine, since they often allude to the occurrence of pains in the joints after dysentery.[5] Sydenham[6] expressly mentions its occurrence as a sequela of dysentery, in 1672; Stoll[7] observed it at a later date. The occurrence of rheumarthritis as a sequela of epidemic dysentery has been not unfrequently noticed during the present century, both in France (Thomas, Cambray, Trousseau, Delioux de Savignac, Huette,[8]) and in Germany (Braun, Witowsky,[9] Gauster,[10] Kräuter,[11] Rapmund).[12]

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[1] Dublin Journal of Medical Science. 1872. III., 98. February.

[2] *Pitha* u. *Billroth's* Chirurgie. II., 2. S. 504.

[3] *Chomel's* Lectures, p. 100.

[4] *Trousseau*, Clinical Lectures, Vol. IV., p. 443. (New Sydenham Society's translation.) See also *Betz*, Ueber die Scharlachkrankheit und den Rheumatismus. Jahrb. für Kinderheilkunde, XVI., 336; also *Blondeau*, in Archives générales, September, 1870.

[5] *Hippocrates* (Praenotiones, ed. Kühn, 1825, p. 311), says: "Intempestive suppressa intestinorum difficultas (dysenteria) abscessum in costis, aut visceribus aut articulis inducit." Similarly, *Caelius Aurelianus*, De Morb. Chron., IV., Cap. 6.

[6] Loc. cit., Cap. IV., p. 192.

[7] Loc. cit., III. De naturâ dysent.

[8] For the literature on this subject, see *Quinquaud*, Gaz. des Hôpitaux, 1874. Nos. 54, 56, 82, 83.

[9] See *Volkmann*, loc. cit., 503.

[10] Memorabilien. 1869, p. 56.

[11] Die Nachkrankheiten der Ruhr. Cassel, 1871.

[12] Deutsche Klinik. 1874, No. 17.

As regards certain other predisposing causes, specially alluded to in the works of older authors, it may be said that their influence is either very doubtful (*e. g.*, that of temperament), or else admits of being explained by reference to some of the causes already mentioned, *e. g.*, the special liability of vigorous subjects may be due to their following those callings which have previously been mentioned as peculiarly liable to the disease.

Finally, there exists a traditional belief that a predisposition to rheumarthritis may be inherited. This belief is chiefly based on facts observed in relation to gout (Chomel); still, there are some recent observations specially concerning rheumarthritis (Fuller, Lebert, Picot) which ought undoubtedly to stimulate us to further inquiry.

Among the exciting or accidental causes of the disease, chilling of the surface takes a foremost place. It is especially to sudden cooling of the body when heated by exertion, exhausted and perspiring, that the onset of polyarthritis must be ascribed. In the majority of cases (according to Lebert, in rather more than half the total number), the statements made by patients are so precise as to leave no room for doubt as to the existence of a causal connection between the actual chill and the disease that broke out immediately afterwards.

Every physician can furnish illustrations from his own experience. I need, therefore, only mention a few very striking ones. A boy was struggling with one of his comrades in the school-room; an inkstand was upset and its contents splashed over the seat at the moment when the master entered. The boy, overheated by his previous struggle, sat down directly in the pool of ink, which soaked through his trousers. On the very next day he was seized with polyarthritis. Another boy fell ill in much the same way twenty-four hours after he had been drenched by a sudden shower on his way home from a lesson in gymnastics. I have repeatedly seen ladies attacked by the disease after exposure to a draught when overheated by dancing.

Opportunities of catching cold are more abundant during the bad season of the year, particularly in spring and autumn, with their frequent and sudden changes of temperature. Hence the greater prevalence of polyarthritis at such times, and the special liability of those occupations which expose the body to sudden variations of temperature.

There is, however, a large residue of cases in which neither a chill nor any other exciting cause can be discovered. In a few of the cases which have come under my own notice the outbreak of the disease followed closely upon severe emotional disturbance (fright); the patients had been greatly overheated at the moment, but steadily denied having been exposed to any source of cold.

For instance, a young lady was attacked by polyarthritis the day after she had been much frightened by an outbreak of fire (which was instantly put out) in a ball-room where she was dancing.

In what way chill—that most common of the exciting causes of the disease—produces rheumarthritis, what may be the sequence of changes between the initial abstraction of heat and the actual outbreak of the malady, we do not at present rightly know. Various theories have been suggested to explain their connection, and to throw light upon the essential nature of the phenomenon of "chill" itself; but they are all of them inadequate. Various attempts have been made to connect the articular inflammation with the cardiac complications, especially since the frequency of the latter has been recognized. Some have chosen to view the articular and cardiac disorders as co-ordinate effects, immediately resulting from the operation of an "arthritic" or "rheumatic" principle, endowed with a special affinity for the connective tissues and serous membranes, and thus exciting inflammation, now in the joints, now in the endo- and pericardium, now in the pleura, etc., or in several of these at once or successively. Others, again, prefer to look on the heart-disease—the endocarditis—as the primary change, and on the articular disorder as its consequence, resulting from embolism by particles of extreme minuteness washed off from the endocardium of the left ventricle (mitral valve). This view was first advanced—so far as I have been able to ascertain—by Pfeufer. Hueter has recently attempted to establish it more firmly[1] by showing that endocarditis may be present without giving rise either to subjective or objective symptoms; he then suggests that it may very well precede the inflammation of the joints in rheumarthritis, even though not recognized till afterward; moreover, its presence in a latent form must be assumed in those cases also which appear to run their course without any cardiac complication. Hueter compares the joint-affection in polyarthritis with the cutaneous hemorrhages in purpura hemorrhagica (peliosis rheumatica); the latter have also been referred to an embolic origin, and are not unfrequently associated with swelling of the joints. However enticing this theory may appear at first sight, there are some great difficulties in the way of adopting it. Even if we grant that in the great majority of cases of polyarthritis (about two-thirds of the entire number) in which we fail to recognize the existence of endocarditis, or in which no valvular mischief is subsequently developed, endocardial inflammation nevertheless exists; even if we admit (though without being able to explain the fact) that a latent endocarditis of this sort is specially prone to occur in connection with the polyarthritis of middle and advanced life (when endocardial mischief is more rarely diagnosed than in youth); even if we admit all this, I say, we shall still be confronted by the surprising fact that in this latent form of endocarditis the minute emboli should be impacted only in the vessels of the synovial membranes, and never, or hardly ever, in those organs which are primarily and most frequently exposed to the chances of embolism in other forms of endocarditis, viz., the spleen, kidneys, brain, retina, bowel, etc. Inasmuch as the emboli, which are supposed to excite inflammatory changes in the joints, must be endowed with specific phlogogenic powers, they should give rise not to mere hemorrhagic infarctions, but to embolic abscesses, both here and even in other organs unprovided with "terminal arteries,"[1] since the emboli are, *ex hypothesi*, of the smallest possible dimensions. In a word, every case of polyarthritis ought to run the course of an ulcerative endocarditis. This, fortunately, is not the rule. Or must we believe that the phlogogenic action of the emboli is limited to the joints, while in other organs they operate either mechanically or not at all? The organ which, next to the joints, the heart, and perhaps the pleura, is most frequently affected—using the term in a relative, not an absolute, sense—is the brain. But the symptoms of cerebral disturbance, when they do occur, are very unlike those usually produced by embolism, whether of the arteries or capillaries; on the contrary, they are due, with few exceptions, to the rapid elevation of temperature, with which they coincide in point of time. Hueter's theory would thus compel us to assume, in most cases of rheumarthritis: first, the presence of an endocarditis absolutely latent as regards its usual symptoms; secondly, a peculiar immunity of all the organs, except the joints, from the usual effects of embolism, an immunity wholly without parallel in other forms of endŏcarditis. Now, such assumptions as these transcend the limits of justifiable hypothesis. Finally, as regards the so-called purpura rheumatica, it is quite possible that the cutaneous hemorrhages may, in many instances, be really due to embolism; but the joint-affection which frequently accompanies them has nothing whatever in common with rheumatic polyarthritis, just as, conversely, purpura is very rarely met with in true polyarthritis.[1]

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[1] Klinik der Gelenkkrankheiten, *loc. cit.*; also *Hotop*, Inauguraldissertation, Greifswald, 1872.

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[1] "Endarterien." See *Cohnheim*, Untersuchungen über die embolischen Processe. Berlin, 1872, p. 98.

Accordingly, we must reject the theory which derives the articular inflammation from a previous endocarditis. That theory is based on insufficient grounds. Moreover, it offers no explanation of the *nexus* between the chilling of the surface and the initial endocarditis, or the disease as a whole. Hueter, indeed, has recently hinted in general terms at the possibility that, when the body is heated and the superficial vessels dilated, the monads (micrococci) present in the atmosphere may find a more easy entrance into the organism, and that many cases of "chill" may thus be accounted for.

In relation to this question—putting aside the vague or unsupported speculations of older authors—there are only two explanatory theories which are entitled, in the present state of our knowledge, to be discussed. Moreover, they do not exclude —indeed, they may even be made to supplement—each other.

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[1] Cf. *Scheby-Buch* in Deutsch. Archiv f. klin. Mediz. XIV., p. 466.

The first of these theories, whose main outlines were long ago sketched out by Froriep[1] and Canstatt,[2] views the articular affection as the result of a disturbance of innervation, consequent on peripheral irritation set up by a chill. To bring this theory into agreement with our present notions of pathology, we must suppose either that the abstraction of heat affects the trophic and vaso-motor nerves of the joints directly, thereby exciting inflammatory disturbance in them, or else that it operates as an irritant upon a variable number of the peripheral expansions of centripetal nerve-fibres, through which the irritation is conveyed to the vaso-motor and trophic nerve-centres, exciting them to abnormal activity. The latter hypothesis, which assigns a central origin to the joint-mischief, has more in its favor than the former one. It agrees better with the shifting character of the disorder; and the possibility of an irritation in the central organs of the nervous system being suddenly propagated to the central origin of nerves supplying the most divers tracts, is supported by analogy. Take, for example, the observations which have been rapidly accumulating of late years as to the dependence of certain joint-affections on chronic inflammatory changes in the spinal cord (cf. Arthritis deformans). Take, again, the various experimental data which lead us to infer that the cord sympathizes more deeply with irritation and inflammation of peripheral nerves than used formerly to be supposed. On the other hand, our knowledge concerning trophic nerve-fibres is still too uncertain to allow us to view this theory as anything more than a hypothesis,—though a hypothesis not in contradiction with any known fact. Above all, we have no evidence to prove that multiple inflammation of the joints can be produced by a single or repeated irritation of peripheral nerves.

The above theory makes no attempt to define the nature of the irritation set up by chill. Now, the second theory to which I have alluded is competent to supply this missing link. It looks for the noxious principle in some alteration in the composition of the blood and humors,—more especially the abnormal development of an acid. Lactic acid has actually been specified as the cause of the morbid phenomena; and both Richardson[1] and Rauch[2] have tried to demonstrate the occurrence of serous inflammations after the injection of lactic acid in dogs and cats. This chemical theory has grown out of older speculations on the retention in the system of certain acrid humors, owing to disordered function of the skin. Hitherto, however, it has rested on no surer basis than the observed facts of the strongly acid reaction of the urine and sweat in rheumarthritis. It has never met with much favor in Germany; indeed, it has lost what little credit it once enjoyed, since Möller[3] and Reyher[4] proved the results of the above-mentioned experiments to be erroneous. With all this, however, the theory in question has a great deal to support it. It merits some consideration, were it only because of its superiority to all its rivals in stimulating inquiry and furnishing new points of view.

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[1] Die rheumatische Schwiele. Weimar, 1843.

[2] Spec. Pathologie und Therapie. 1847, II., 2, p. 609.

Great stress ought to be laid, in the first place (as Corrigan justly insists), on the fact that the chill operates injuriously on the body when the latter is heated and tired by exertion. This is in agreement with the pathological law, according to which every organ is most liable to become affected by disease when it is engrossed in or exhausted by its functional activity. Setting out from this fact, we must allow any hypothesis a hearing which attempts to establish some connection between the articular inflammation brought on by chilling the body when overheated and the abnormal accumulation of acids (*e. g.*, lactic acid) in the system. For, 1. During bodily exertion the joints are, next to the muscles that move them, the most functionally active parts; hence, they must stand second only to the muscles in their liability to disease. True, we are little used to think of the joints in connection with functional activity and nutrient processes—we are disposed to think of them as wholly passive; but this attitude of mind is undoubtedly due merely to our ignorance concerning these neglected organs, in regard to which Hueter appropriately observes, "that, in comparison with other organs of equal or similar importance, they have been treated by modern investigation in the field of anatomy, physiology, and development, as step-children." The solitary fact that is known to us concerning physiological changes in the articular contents—the increased concentration of the synovial fluid during exercise, when the proportion of mucin, albumin, and extractives is nearly doubled, as pointed out by Frerichs[1]—is enough to show that the joints, like other organs, may be the seat of very active nutritive changes.

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[1] The Cause of the Coagulation of the Blood. London, 1858, p. 371.

[2] Ueber den Einfluss der Milchsäure auf das Endocard. Dissert. Dorpat., 1860.

[3] Symbolae ad theoriam rheumatismi criticae et experimentales. Habilitationsschrift. 1860. Königsberg und Königsb. mediz. Jahrb. 1860, II., p. 277.

[4] Zur Frage der Erzeugung der Endocarditis u. s. w. Virchow's Archiv, XXI. 1861, p. 85.

2. A formation of acids and acid salts, of lactic acid and acid potassium phosphate, takes place during muscular exercise, and it is to the accumulation of these products that muscular fatigue is due (J. Ranke, Roeber). Under ordinary circumstances, these products are undoubtedly eliminated; the lactic acid, more particularly, is partly oxidized and got rid of as carbonic acid and water; partly—when there is a great deal of it—excreted unaltered in the sweat.[2] Now, should the cutaneous surface be chilled, the elimination of these substances will be checked, and they will necessarily accumulate in the system until they can be otherwise excreted or decomposed.

We thus have certain knowledge of the presence of at least two pathogenic factors whenever the body, heated and perspiring from exertion, is suddenly chilled: on the one hand, the joints are specially predisposed to disease; on the other, an abnormal amount of certain acids and acid salts, especially lactic acid, is accumulated in the system. The next point is to determine whether a causal *nexus* can be shown to exist, or as likely to exist, between these two tendencies—whether the accumulation of waste products may, on occasion, give rise to articular inflammation. I have already stated that the experimental demonstration which Richardson tried to furnish, by injecting lactic acid, proved a failure; I may add that it would have been most surprising had it been otherwise, *i. e.*, had the attempt to produce artificial rheumarthritis in rabbits, cats, and dogs succeeded—animals which are by nature either wholly insusceptible, or very slightly susceptible to the disease. Experiments of this sort could only have been expected to succeed if they had been conducted on animals such as the horse, which are naturally liable to rheumarthritis, and which, be it said in passing, resemble other beasts of burden and the human subject, in perspiring, *i. e.*, in furnishing a specific secretion from their sudoriparous follicles during muscular exertion. True perspiration cannot take place in cats, dogs, or rabbits, for these animals are destitute of sweat-glands.[1] Foster, moreover, has recently published some observations conducted on the human subject, which prove, in a more striking way than any experiments on the lower animals could possibly do, that a disease completely analogous to polyarthritis may be produced in man by the administration of large doses of lactic acid.[2] Foster's observations were made on two diabetic patients, in whom the prolonged administration of lactic acid invariably produced the disease in a perfectly characteristic form, the symptoms always subsiding when the medicine was discontinued. Kuelz[3] has quite recently observed the same phenomenon in a diabetic patient who was being treated with lactic acid. These facts do not lose any of their force from the argument that other persons, both sick and healthy, may take even larger doses of lactic acid without injury; this would merely indicate that individual predisposition is a necessary factor in the causation of the disease. But the individual predisposition itself may be due either to a peculiarity of constitution—a lack of power to resist certain definite noxæ, etc., or it may be acquired at the time by violent muscular exertion.

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[1] Wagner's Handwörterbuch der Physiologie. III., p. 463.

[2] Lactic acid has been found in the perspiration by *Favre*, while *Schottin* and *Funke* failed to discover it. Their failure may possibly have been due to previous decomposition of the acid into butyric and propionic acids; or it may have eluded their search, owing to the quantity of perspiration subjected to analysis having been insufficient. Finally, the discrepancy may be accounted for by supposing that while the one observer dealt with the secretion of the sweat-glands after exertion, the others may have analyzed only the condensed water exhaled from the surface of the skin.

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[1] I have referred elsewhere (*Virchow's* Archiv, XLV., p. 375, and Untersuchungen über den fieberhaften Prozess. Berlin, 1873, p. 164) to the relation between the perspiratory function and the muscles.

[2] The Synthesis of Acute Rheumatism. Brit. Med. Journal, 1871, 21 December.

[3] Beiträge zur Pathol. und Therapie des Diabetes u. s. w. II., 1875, p. 166.

The above considerations appear to me to indicate that the theory of an accumulation of lactic acid in the system deserves more attention in relation to the pathogeny of rheumarthritis than has been hitherto accorded to it. It is well worthy of being further tested both by experiment and by clinical observation.

The objections which have been brought against chemical theories of rheumarthritis are either illogical, or they fail to touch the particular theory I have just described. It is commonly urged that lactic acid has not yet been demonstrated in the sweat and urine of patients suffering from polyarthritis. But this proves nothing, for in the first place lactic acid has not often been looked for, and when it has, not with the necessary care. I know of only one statement on the subject, that made by Lehmann,[1] to the effect that he was unable to discover it in the perspiration of "rheumatic or gouty" patients and of puerperal women, though others had found it in the sweat in cases of puerperal fever. Now, as lactic acid readily becomes decomposed in the perspiration, its recognition may easily fail. Then, again, there is no reason to believe it necessary that a *materies morbi* should be eliminated as such during the progress of the disease; this is a notion which dominated the older medicine; it used to be thought that some injurious product or acrid humor was generated in the system, and kept up the disease until it had in one way or another been got rid of. Nowadays we are quite able to conceive that the material cause of the disease may be destroyed after it has initiated certain processes, or else may remain dormant in the body; that—to pass from the general to the particular—the lactic acid, after having done its work, may be oxidized into carbonic acid and water. Just as the discovery of the acid in the secretions would furnish no conclusive proof that the chemical theory of the disease was the correct one, since the acid might very well happen to be a product and not the cause of the morbid process, so we have not the slightest ground for regarding the absence of lactic acid from the secretions as conclusive against the chemical theory, more especially when we reflect that the acid in question has never yet been adequately looked for.

Another objection is often urged against this theory. It is said that in the course of certain hydropathic procedures the skin is often made to perspire abundantly, and then suddenly and energetically cooled down by cold affusion, wrapping in wet sheets, etc. This objection rests upon the mistaken assumption that the secretion of the sweat-glands poured out after violent muscular exertion, is identical with the liquid that collects on the skin of a man exposed, while at rest, to the influence of a hot bath or of hot air saturated with moisture. The latter certainly goes by the same name as the former; but it consists, for the most part, of condensed watery vapor which has been exhaled from the skin, and contains extremely little of the specific constituents of the perspiration. To check the elimination of this fluid cannot, therefore, be the same as to check true perspiration caused by exercise. The former proceeding may be free from risk; the latter, as daily experience proves, is very seldom harmless. Moreover, the absence of any evil consequence—nay, the beneficial effects that result—from the hydropathic measures above alluded to, may perhaps be explained by the energetic efforts made to revive the activity of the skin, just after it has been cooled, by friction with a flesh-brush, etc.

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[1] Lehrbuch der physiolog. Chemie. II., 335.

Finally, a third objection is based on the results of experiments made on animals. When the cutaneous functions are suppressed in them by varnishing the skin, a train of phenomena ensues wholly different from those ascribed to chill. This objection has no *locus standi* if meant to apply to the explanation of rheumatic disorders; for varnishing the skin of an animal is no more analogous to chilling of the surface than extirpation of the kidneys or ligature of the ureters is analogous to temporary retention of urine. By varnishing the skin we *permanently* suppress the function of an organ essential to the continuance of life—no kind of chill does anything like this; and the mere fact that an animal dies when it has been varnished proves that no other organ, whether kidney or lung, either singly or jointly, is capable of doing the work of the skin; further, that the skin has some important function to perform besides the elimination of water and carbonic acid—a function which, unlike this, cannot be performed by deputy. There is yet another reason why such varnishing experiments should throw no light upon the chemical theory developed above, for of the condition presupposed by the latter (violent muscular exertion) there is no word in any of the experiments. Moreover, these were, for the most part, conducted on animals devoid of any natural liability to polyarthritis. Lastly, the results of such experiments cannot be transferred to the human species, for varnishing the human skin seems to be a perfectly innocent operation.[1]

Our way of looking at the subject enables us, further, to account better for those cases in which an emotional shock, instead of a chill, has been experienced by the heated and perspiring organism, for it is well known that a shock of this kind is able to arrest perspiration in a moment. Even when perspiration is suppressed by the *sudden* chilling of only a small area of the perspiring skin, there is every reason to believe that the glandular activity is inhibited by a reflex mechanism, assisted by a psychical impression.

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[1] Cf. *Senator:* Untersuchungen über den fieberhaften Process. P. 196, seqq.

This is not the place to inquire how far the two mutually complementary theories just enunciated are capable of throwing light on other disorders caused by chill. It may, however, be stated that they are capable of being applied to certain rheumatic affections of the muscles, no less than to the inflammation of the joints—to those, *e. g.*, which are due to .chilling of the surface during or immediately after violent exertion. They may likewise serve to explain certain disorders of motor nerves (spasm and paralysis) due to the same cause,—of nerves which have undoubtedly been in a state of active functional excitement during the previous muscular exertion, and which are consequently predisposed to disease. There still remain, however, a number of affections due to chill, *e. g.*, those which arise during absolute, or all but absolute, repose of the muscular system, which our theory cannot explain at all, or not without the aid of more or less arbitrary assumptions. These affections are some of them capable of being explained in another way (*e. g.*, many affections of the mucous membranes); others, again, are utterly inexplicable by the light of our existing knowledge; among the latter we must place that relatively small group of cases of polyarthritis for which no exciting cause can be discovered. These cases must be left, for the present, unexplained.

Whether acute rheumatic polyarthritis ought to be regarded as a constitutional disease, localizing its action in the joints, or as a purely local articular affection, can hardly be regarded as an open question at the present day. The implication of joint after joint for days and weeks after the exciting cause of the malady has ceased to operate, the characteristic sweating, the frequency of cardiac complications,—these features are all of them foreign to articular inflammation arising from local causes. The fact that the pyrexia precedes the articular disorder in time may be adduced in support of the view that polyarthritis is a constitutional disease. But this fact admits of another interpretation. It may be said that the joints are really affected before the fever sets in, but that the articular affection is not sufficiently advanced to enable us to recognize its existence.

LEEDS & WEST-RIDING
-CHIRURGICAL SOCIETY

Pathology.

General Outline of the Disease.

The outbreak of rheumarthritis is usually preceded by a few trivial symptoms of an indefinite kind, such as general *malaise*, dragging pains in the limbs, etc. These last but a short time, seldom more than two or three days. The real onset of the malady dates from the first rise of temperature, which is sometimes ushered in by a single rigor, more or less marked, sometimes by slighter and repeated attacks of shivering. The first elevation of temperature is usually moderate, not exceeding 40° C. (104° F.). Roughly speaking, the rise of temperature is proportionate to the number of joints affected and the intensity of the articular inflammation. Other symptoms of fever show themselves at the same time. The head may be affected; the patient complains of thirst and loss of appetite; the pulse and breathing are quickened. These symptoms are all of moderate intensity, corresponding to the not excessive elevation of temperature. On the same, or, at latest, on the following day, one or other of the joints—usually of the lower extremity—becomes painful, and, when sufficiently near the surface, hot, swollen, and more or less distinctly reddened as well. The patient is afraid to move the affected limb; he feels even the slight weight of the bed-clothes. Soon, moreover, we are able to detect fluctuation in the joint, when its anatomical position allows of its being examined, as, *e. g.*, in the knee, elbow, and shoulder-joint. After a brief interval—the fever either remaining stationary or undergoing a slight increase—fresh joints become involved, while in those originally affected the inflammation usually subsides: usually, but not always. They may, in rare cases, continue swollen and painful, or, after a short interval of health, they may become inflamed anew. In this way most of the joints in the body may be successively affected; and, when the disease is localized in the larger articulations, such as the knee, hip, shoulder, and intervertebral joints, the patient is in a really lamentable predicament. He suffers agony when he tries to pass water, when his bowels are relieved, when his linen is changed. He lies motionless in bed, and the slightest vibration makes him cry out. We often find the pain very acute without any corresponding severity in the other signs of articular inflammation; exacerbation frequently occurs without obvious cause, especially (in the opinion of many writers) towards evening; the inflammation often extends from the joints to neighboring parts, to the tendons and muscles, and perhaps even to the nerves. We not unfrequently see swelling and œdema all round the affected articulation.

The skin does not feel very hot to the touch. In spite of the fever, it is usually bedewed with perspiration, which has a sour odor, and often raises the cuticle in minute vesicles (sudamina). Other forms of eruption are likewise not uncommon. The urine is scanty, concentrated, and of high specific gravity; it is strongly acid, and soon lets fall a sediment of brick-red urates and free uric acid. The tongue is moist and coated with a whitish fur; the bowels are usually confined; the fæces, even at the height of the disease, are usually more dry and hard than in health, or than they are in other patients kept on the same diet; this is due to the abundant exhalation of water through the skin.

Apart from some rare exceptions, to be alluded to hereafter, the patient's mind remains unclouded during the whole course of the disease. Delirium is either absent altogether, or there may be a little wandering, in specially sensitive and irritable patients, when the fever undergoes an exacerbation. Sleep is greatly interfered with by the severity of the pain; indeed, sleeplessness and pain in the joints are often the only symptoms of which the patient complains; occasionally the abundant sweating is an additional source of annoyance.

So the disease may go on for weeks (in the absence of complications) without following any typical course, its local manifestations (*i. e.*, the number of joints affected and the violence of the articular inflammation) undergoing alternate exacerbation and remission, until at length no fresh joints become inflamed, the fever and sweating abate, together with the pain in the joints already affected, and recovery ensues. The joints which have been inflamed may recover completely, or, in less favorable cases, some residue of the inflammatory process may be left in them. As a rule, acute polyarthritis runs its course in from three to six weeks; but after recovery, the joints may remain peculiarly susceptible for a considerable time, showing a tendency to renewed inflammation, by which the progress of convalescence may easily be interrupted. But even apart from such interruptions, convalescence from a severe attack of rheumarthritis is generally very slow; the patient is usually much reduced, chiefly, in all likelihood, owing to the amount of water which has been got rid of through the skin.

Simple (uncomplicated) rheumarthritis seldom terminates in death. The fatal issue, when it does occur, is commonly preceded by a rapid elevation of temperature, with all the signs of a profound disturbance of the nervous centres—delirium, an enormously quick pulse—speedily followed by deep coma and collapse.

The above description corresponds to cases of the disease which are of great or medium severity. But the disease may assume a different form. Sometimes, in its earlier stages, or even throughout its entire course, only a few joints are affected, and these only in a moderate degree. In such mild cases the fever and other disturbances are proportionate to the local mischief, and are very slight; the temperature, especially in the morning, scarcely rises above the normal; the appetite and sleep are but little interfered with, and the disease may subside in a comparatively short time (from eight to fourteen days). But it may pass, at any moment, into a graver form by the implication of fresh joints in the inflammatory process. Other deviations from the normal type may be caused by the supervention of complications, which are more numerous and more various in this than in any other disease, and which tend to modify the course, duration, and especially the issues of rheumarthritis. True, even the complications seldom lead to death; but they often prevent complete recovery by leaving behind them a residue of incurable organic mischief, to which the patient succumbs long after the polyarthritis has disappeared.

LEEDS & WEST RIDING
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Morbid Anatomy.

Since acute polyarthritis, *per se*, is rarely fatal, an opportunity of studying the structural alterations to which it gives rise does not often occur; and when it does occur, the special changes found are so trifling that they only serve, for the most part, to confirm the observations made on the patient during life, without adding anything to our knowledge concerning the essential nature of the disease. Many of the statements made by older authors in reference to structural changes caused by rheumarthritis are based upon a mistaken diagnosis; pyæmia, glanders, cerebro-spinal meningitis, etc., have been mistaken for, or else classed with, rheumarthritis. As regards the joints more particularly, the phenomena, which, during life, indicated with certainty the presence of an acute inflammatory process, are often very indistinct after death; even an exudation abundant enough to distend the capsule of a joint to the utmost during life may have almost entirely disappeared after death. Hence it is that most of the facts that have been recorded about acute rheumatic inflammation of the joints, and which I am myself about to describe, have been gathered less from the direct inspection of such joints, than from the study of other varieties of articular inflammation, especially such as have been artificially induced in animals, most of them being of a purulent order.

In proportion to the violence of the inflammation and to the stage it may have reached, we find the synovial membrane more or less vividly reddened in patches. The vessels are injected, especially in the villous processes and the so-called glands of Havers; the injection is also well marked in the ring of vascular loops and arches situated at the junction of the synovial membrane with the cartilage. Small hemorrhages may often be detected with the naked eye, or, more readily, with a lens. The internal surface of the membrane is granular and cloudy; it has lost its lustre; here and there it may present a thin and easily separable coating of fibrinous exudation; its tissue appears swollen and thickened. The superficial layer of cells is partly detached; where it still continues to adhere, the corpuscular elements of the intima are seen to be distended with a coarsely granular protoplasm instead of their usual scanty and finely-granular contents (Hueter). The lymphatics of the synovial adventitia are greatly dilated, and thus brought so close to the intima as to be covered in by only a single layer of its cells. (C. Gerlach, Hueter). The articular cartilages, as a rule, are rarely œdematous ; when active suppuration has been going on, they may be necrosed. The perisynovial connective tissue likewise takes part in the inflammatory process, when this is at all severe; we find it œdematous and more or less permeated by pus-corpuscles. The bony epiphyses, too, together with the cartilage that covers them, appear abnormally vascular. Finally, the soft parts about the joint are variably congested and œdematous, occasionally studded with minute extravasations. In many cases the inflammation is found to have spread to the sheaths of the tendons and the bursæ mucosæ, whose serous and sero-purulent contents are found to be increased.

Disorganization of the joints of a more profound character, such as abscess-formation, ulceration, necrosis of cartilages, etc., does not come under consideration in connection with rheumarthritis, but among its possible sequelæ.

The amount of fluid found in a joint after death does not always correspond, as I have already stated, with the amount recognized during life. It may vary from a few drops to many grammes, and differs from ordinary synovia (which is viscid and glutinous, owing to the mucin it contains) chiefly by its greater fluidity. It usually resembles a serous exudation of a cherry-colored or reddish hue, rendered turbid by the admixture of flocculent and gelatinous coagula. It has an alkaline reaction, is rich in albumin and fibrin, and may be seen, under the microscope, to contain—besides the detached and more or less altered elements of the synovial intima—a variable number of red blood-discs and pus-cells. When the latter happen to be abundant, the fluid in the joint approaches the naked-eye and microscopical characters of pus. The presence of true pus, however, is quite exceptional in rheumarthritis, just as any considerable admixture of blood has only been met with occasionally in very severe cases complicated with hemorrhagic tendencies due to other causes. An articular inflammation attended by exudation, either wholly or principally fibrinous, has been described by many writers (Arthromeningitis fibrinosa s. crouposa); but it is doubtful whether this form is ever met with in rheumarthritis.

We have very little precise knowledge about the chemical composition of the exudation. Laboulbène examined the fluid from two knee-joints. The proportion of dry solids amounted to 56.46 and 65.63 parts *per mille;* that of ash, to 8.6 and 8.2 parts *per mille;* the fluid also contained mucin.[1] In an exudation from a joint affected by gonorrhœal arthritis, Méhu[2] did not succeed in finding any mucin.

According to Andral and Gavarret, the blood is very rich in fibrin, containing as much as one per cent. of this substance, and even more. Becquerel and Rodier found the serum to contain less than its due proportion of solids. The blood is usually firmly coagulated after death; it is dark and fluid only in such cases as prove rapidly fatal with a sudden rise of temperature. In one case observed by Lebert (loc. cit., p. 53) the blood contained an excess of urea. We do not know anything more, of a definite kind, about the alterations taking place in the blood during rheumarthritis. The abnormal development of an acid (lactic acid, according to Todd, Fuller, Bouchardat, et al.) in the blood during life has often been assumed, but never proved to occur.

Complications, especially with disease of the thoracic viscera, are usual. Otherwise, the organs present either no appreciable alterations whatever, or alterations of an inconstant and indefinite kind. Thus, for example, in those cases which run their course with a high temperature and severe cerebral symptoms, parenchymatous degeneration of particular organs, a swollen condition of the hepatic cells and renal epithelia, are said to have been found, the brain itself being either wholly free from morbid change, or else markedly congested, with minute extravasations or a variable amount of œdema in the pia mater and arachnoid.

Finally, the skin may show traces of eruptions present during life.

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[1] *Laboulbène* in Arch. gén. de Médecine, August, 1872, p. 150.

[2] *Méhu*, Bulletin de l'Acad. de Méd., 1872, No. 22.

Analysis of Individual Symptoms.

Condition of the Joints.

The inflammation is scarcely ever limited to a single joint, though in mild cases of the disease, attended with but little fever, we may find a single joint greatly inflamed, while several others are affected in a very minor degree. As a general rule, the larger joints are alone attacked; the smaller ones—those of the toes and fingers—remaining free. The disease is never limited, throughout its entire course, to the smaller joints. As the inflammatory phenomena in any particular joint usually last for several days (two, four, or even longer), fresh joints becoming implicated in the meantime, we usually find several of the joints affected simultaneously, when the case is at all severe. In this way, eight, twelve, or even more joints may be affected at once towards the end of the first, and during the second and third weeks of the disease.

The knee and ankle are the joints most frequently attacked; next in order of frequency come the wrist, elbow, and shoulder; next, but at a great interval, the hip and finger-joints; then those of the spinal column, of the toes, the sterno-clavicular articulation, and that of the lower jaw. Finally, Schuetzenberger and Liebermann[1] have observed inflammation of the laryngeal articulations (crico-arytænoid).

Monneret found, in 93 cases of the disease, that the knee-joint was affected in 69, the wrist in 49, the ankle in 41, the shoulder in 19, the hip in 8, etc.

The functional disturbance and degree of suffering vary with the position and importance of the affected joints. The greatest amount of trouble is caused by inflammation of the intervertebral joints, as it condemns the patient to absolute immobility. In the case of any other joint, he tries instinctively to place it in that position which inflicts least strain upon it; the knees and elbows are flexed; the hip likewise; the hand is usually kept quite straight; the foot slightly bent towards its plantar aspect.

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[1] Union Médicale, 1873, No. 153. Gazette des hôpitaux, 1873, No. 136.

Besides the local swelling, redness, and fluctuation, of which I have already spoken, and which depend upon the degree of inflammation and the more or less superficial position of the joint, we may often perceive grating and crepitus on movement,—sounds of which the patient is himself aware. They are generated partly in the interior of the joint, partly in the sheaths of the neighboring tendons which are implicated in the inflammatory process, and are due to the admixture of a variable proportion of fibrinous flocculi and deposits with the exuded liquid.

The signs of inflammation often disappear quite suddenly from one or more joints, *e. g.*, during a single night—other joints, or else internal organs, being attacked with equal suddenness. This may be explained in one of two ways. We may suppose that some phlogogenic matters, endowed with a special affinity for the joints and certain serous membranes, and with a special tendency to cause exudations of serous fluid, are introduced into, or generated in, the system *intermittently*. Or we may imagine that various trophic centres, specially related to particular joints, are successively attacked. It is to its pre-eminently serous character that the exudation owes its capability of being readily absorbed; hence, too, the rapidity with which the local symptoms may disappear.

According to Lebert, the synchondroses—more especially the sacro-iliac and pubic—are sometimes affected as well as the true joints.

The State of the Skin.

The skin feels hotter than usual; but it does not, as a rule, exhibit the same pungent heat as in other febrile maladies, because it is almost always covered with perspiration. The copious sweating, which forms one of the most constant symptoms of rheumarthritis, is wholly devoid of critical significance; it is a part of the morbid process, like the articular affection. It tends to subside rather earlier than the inflammation of the joints, usually following the course of the pyrexia; it reappears when, as often happens, a recrudescence of the disease takes place. The perspiration has a sour smell and a decidedly acid reaction ; it is only where the secretion is allowed to stagnate (as in the arm-pit or between the toes) that its reaction may be found neutral or even alkaline, from decomposition of the urea contained in it into carbonate of ammonia. Large doses of alkalies may produce the same effect. Further details concerning the composition of this morbid variety of perspiration are few in number, and chiefly borrowed from writers of a former generation. They are based on researches wanting in precision, and dominated by certain humoral theories. Todd thought that an excess of lactic acid was got rid of in the perspiration ; but Lehmann's[1] search for the acid proved fruitless. Wolff and Starke asserted that they found uric acid and urates in the sweat. Anselmino demonstrated the presence of albumen; but Leube[2] has since shown that this substance may be found in the perspiration under other conditions also.

Owing to the copious sweating, various eruptions frequently break out upon the skin. *Sudamina* are simple vesicular elevations of the cuticle; they are often associated with *miliaria* (*rubra*), undoubtedly caused by the irritating effect of the copious secretion upon the skin. *Urticaria* is not unfrequently observed. Lebert saw it in two of his cases ; I have seen it last, in one case, for two days during the second week of the disease, when it was at its worst. In another case, that of a boy of six, the rash made its appearance a day or two before the outbreak of the malady. A similar sequence was also noticed by Macario in two out of forty-five cases. *Herpes labialis* is occasionally met with during the early part of the disease. Finally, the statements concerning the occurrence of *hemorrhagic purpura* in connection with rheumarthritis rest, in all likelihood, on an error of diagnosis. (Cf. section on Diagnosis.)

State of the Urine and Urinary Organs.

The state of the urine in rheumarthritis is largely dependent on the abundant exhalation of water from the skin and on the febrile disturbance. Its quantity, notwithstanding copious draughts of liquid, is abnormally small, and may sink to 300 c.c., or even less, in the twenty-four hours. The quantity of urine passed may vary greatly from day to day, these variations depending not merely on the degree of fever, the abundance of the perspiration, and the quantity of water drunk, but often likewise upon irregularities in the emission of urine, which the patient endeavors to delay as long as possible, from fear of the pain caused by the necessary movements. The color of the urine, save in very mild cases, is reddish yellow or even dark red; it is abnormally acid, when not neutralized by drugs; its specific gravity is high, varying from 1020 to 1030. These phenomena are due to concentration. The percentage of all the urinary constituents, with the exception of chlorine, is increased. Owing, however, to the great reduction in the quantity of urine passed daily, the total weight of solids excreted remains below the normal average. To this statement there is one important exception. The amount of urea eliminated during the height of the disease, under the influence of the pyrexial tissue-destruction, even when the diet is very poor in albumin, not only attains but often exceeds the average of health. Another consequence of the concentrated state of the urine is its tendency to let fall a sediment; this tendency is more marked in rheumarthritis than in most other diseases. Very soon after the urine is passed, a brick-red deposit, usually containing large crystals of free uric acid in addition to the urate of soda, is thrown down. We do not know whether this separation of free uric acid ought to be ascribed simply to the concentrated state of the urine or to the presence in it of abnormal acids (lactic acid ?). The older physicians were disposed to hold the latter view without sufficient proof, perhaps because it seemed to agree with their belief in an over-production of acid in rheumatic disorders. So, too, it is a question whether the darker tint of the urine is due merely to a uniform increase in the percentage of the normal pigments, or to a special increase of one of them (of urobilin, according to Jaffe[1]), or, finally, to the presence of some abnormal coloring-matters in the secretion.

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[1] Lehrbuch der physiol. chemie. 1853. II. 335.

[2] Centralblatt für die med. Wiss. 1869. No. 39. Also in *Virchow's* Archiv. XLVIII. 181.

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[1] *Virchow's* Archiv. XLVII. 405.

That the presence of a deposit of urates does not imply, as used at one time to be supposed, any increase in the total amount of uric acid eliminated, has been satisfactorily established by the quantitative determinations of Bartels,[1] Hoppe-Seyler,[2] and others.

Small quantities of albumen may be found during one or more days, without the presence of any other sign of renal mischief. The phenomenon is probably due to an increase in the intensity of the pyrexia.

More profound alterations in the kidneys and urinary passages are not usually met with in rheumarthritis. The blister-treatment (to be described hereafter) appears, however, to excite renal irritation and hyperæmia rather more easily than it would do in healthy persons. The urine may contain a good deal of fibrin under such circumstances, and may show a tendency to coagulate when exposed to the air, and even in the bladder, causing thereby some difficulty of micturition.

I have myself[3] seen two such cases of "fibrinuria," and have heard of others in the practice of my colleagues. Similar results have been known to follow the application of blisters independently of rheumarthritis; but not, as it seems to me, either so frequently or so severely.

Corne appears to have met with a case of true nephritis setting in at a later period of the disease, and seemingly of a critical nature; for its development was simultaneous with the disappearance of the articular inflammation. Hartmann, too, has twice seen nephritis come on in the course of rheumarthritis.

State of the Nervous System.

Although most cases of rheumarthritis run their course without any cerebral symptoms—even the headache that accompanies every febrile malady being but slightly marked,—the nervous centres may, in certain unfavorable cases, be variously involved. Acute cerebral or spinal meningitis may set in, or mental alienation, or severe brain symptoms, without any demonstrable lesion of structure, such as are met with in enteric fever and other infective maladies. These various complications used formerly, and indeed up till a very recent date, to be grouped together under the name of "cerebral rheumatism." The first two will be described among the complications of rheumarthritis. The third variety is principally met with in drunkards, or persons whose constitution has broken down from other causes. Such patients usually exhibit a marked degree of excitement from the very first; they become slightly delirious towards evening; they suffer more than is usual from sleeplessness, and this augments their excitement; then, at a comparatively early stage of their malady, towards the end of the first or the beginning of the second week, their temperature, previously moderate, undergoes a great and sudden rise; the skin becomes hot, the abundant sweating often subsides, the pulse is hurried and compressible, the breathing shallow, the sensorium much oppressed, the face cyanotic or pale; and after an interval which is usually very brief—varying from a few hours to one or two days—death ensues. In very rare instances we rescue the patient by reducing his temperature; in a somewhat larger proportion of cases, we may succeed in causing a temporary improvement and delaying the fatal issue.

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[1] Deutsch. Archiv für klin. Med. I. p. 13.

[2] See *Niemeyer's* Pathologie, 1868. II. 540.

[3] *Virchow's* Archiv. LX. p. 476.

The phenomena just described are very similar to those observed to follow the exposure of men and animals to excessive heat, and known as "sunstroke" or "heat apoplexy." In both cases the abrupt rise of temperature is the earliest and most striking symptom of impending danger. Hence, we may reasonably assume that all the other grave symptoms are merely consequent upon the increased heat of the body. The good effects produced by withdrawing this heat lend support to this hypothesis. But, as regards the cause of this rapid elevation of temperature, we can say nothing certain. It may be that the pyrogenic and phlogogenic matters which are undoubtedly present in the blood undergo a great and sudden increase, and paralyze the heat-regulating centres (whose very existence remains to be proved),—or stimulate centres presiding over heat-production; or we may suppose that the primary effect of those substances is to paralyze, or at any rate to weaken, the heart's contractions, and thereby to reduce the amount of heat given off.

I have still to allude to certain paroxysms of palpitation and oppression which not unfrequently occur during rheumarthritis; they are transient, and do not depend on any cardiac complication. They make their appearance when the disease is at its height, with or without demonstrable cause; they may last for an hour or more, and then subside without leaving any trace. During the paroxysm, moreover, the patient exhibits no objective symptoms beyond great acceleration of the pulse and an expression of anxiety and faintness. Accordingly, it is impossible to regard them as the earliest indication of an endo- or pericarditis; their origin must be entirely nervous, a sort of nervous palpitation or stenocardia, possibly brought on by pain and want of sleep. Death may occur during a paroxysm of this kind; but such an accident is rare.[1]

Febrile Phenomena.

I have already stated that the fever is, roughly speaking, proportionate to the number of joints attacked, and to the intensity of the inflammation. It runs no typical course, and is usually moderate in degree.

An initial rigor occurs in barely half of the entire number of cases; it is not usually severe. Generally speaking, several slight fits of shivering, followed by a sense of warmth, are noticed on the first day; at the same time (in all except the mildest cases) the temperature runs up to 39° C. (102.2° F.) or a little higher. Evening exacerbations, occurring on subsequent days, may bring it up to 40° C. (104° F.) or, at the outside, to 40.5° C. (104.9° F.). Wunderlich[2] points out the curious fact that, in an overwhelming majority of hospital cases of acute rheumarthritis, the maximum temperature is reached either on the day of admission or almost immediately after. During the further progress of the malady the temperature obeys no definite rule; it is usually somewhat higher in the evening, but seldom rises over 40° C. (104° F.), except in those fatal cases which I have yet to describe. Periods of remission, or even of complete intermission, lasting for twelve or even for twenty-four hours, are very common; they are always followed by a moderate febrile reaction and an exacerbation of the articular disorder. In this way the disease may come to consist of a series of paroxysms, separated by brief intervals of partial or complete apyrexia. The return of the temperature to its normal level may likewise take place in a variety of ways. A rapid "critical" subsidence is rare. The fall is of a more gradual kind, extending over several days; it may either be uniform or with occasional periods of arrest, or even with momentary exacerbations.

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[1] See a case described by *Rathery* in Gazette des hôpitaux, 1869, No. 57.

[2] Medical Thermometry, New Sydenham Soc. transl., p. 396.

The onset of complications is usually attended by an elevation of temperature; but this is never considerable, save when the secondary disorder is independently characterized by a high degree of fever (*e. g.*, meningitis, and especially pneumonia). The rise of temperature usually precedes the onset of the complication by a short interval; perhaps it would be more correct to say that it is the first symptom to be recognized. When the complications outlast the polyarthritis, the course of defervescence will naturally be modified in accordance with their special nature.

As regards the other phenomena of fever, it is worthy of note that the ratio between the pulse-rate and the temperature is not always maintained, a remarkable quickening of the pulse occurring without any corresponding rise of temperature. This seems to be due to the severity of the pain and the consequent mental excitement, which are often altogether out of proportion to the local symptoms and the amount of fever. There is nothing unusual in the disturbance of digestion; and as regards the pyrexial "alterations of tissue-metamorphosis" nothing is known beyond the fact, already referred to, that the proportion of urea in the urine is augmented, and that an appreciable quantity of this product is likewise got rid of in the perspiration.

As the fever abates the other disturbances abate too; the urine grows more abundant, clear, and bright, the perspiration subsides, the appetite returns, etc.

When the severe cerebral symptoms, already alluded to as being independent of meningitis, happen to occur, the temperature follows the same course as in the first stage of many other acute diseases. Within a few hours it rises to a hyperpyretic level, and then goes on to reach the highest limits ever noticed in the human subject. Th. Simon[1] and S. Ringer[2] were the first to observe and publish cases of this malignant variety of hyperpyrexia; the former putting a temperature of 43° C. (109.4° F.), the latter, one of 43.9° C. (111° F.) on record. Quincke[3] observed a post-mortem elevation of temperature. At death the thermometer showed 44.3° C. (111.7° F.) in the vagina; forty minutes later it indicated 44.7° C. (112.5° F.) in the vagina, and 43.95° C. (111.1° F.) in the axillæ.

Polyarthritis has never been known to run its entire course without fever. But very mild cases of the disease, in which but few joints are attacked and the degree of inflammation is slight, may exhibit only trifling sub-febrile elevations with intervals of complete apyrexia; so that, if the thermometer is rarely used, no rise at all may be detected.

Complications.

There is hardly any disease that presents so great a variety of complications as polyarthritis. They occur both in the more severe and in the milder forms of the malady, though perhaps more often in the former. They may set in either in an early stage, or at the height of the disease; perhaps less often when it is declining. Nay, we sometimes find them setting in simultaneously with the joint-affection, or even preceding the latter by a short interval, so as to make it doubtful which of the two is the primary disease. For these and other reasons,—such as the transient character both of the complications and of the articular mischief, the tendency of various complications to succeed one another,—the older physicians were disposed to ascribe the manifold variety of phenomena to a common cause, a specific *materies*

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[1] Annalen des Charité Krankenhauses. 1865, XIII. 1.

[2] Medical Times and Gaz. 1867, No. 901.

[3] Berlin. klin. Wochenschrift, 1869, No. 29.

morbi, undergoing metastasis from place to place. But as the existence of any such blood-poison still remains to be proved, we of the present generation express ourselves with a semblance of greater precision—though not with any really greater definiteness—than our forerunners, when we say that rheumarthritis is associated with a tendency to disease—especially to inflammation—of internal organs. We are forced to believe that between some of the more frequent complications of rheumarthritis and the articular disorder there must exist a more intimate bond than that by which a disease is usually allied with its complications. This belief appears to rest, first, on the general nature of the disease; secondly, on certain of its individual characters. It matters but little, therefore, whether we view the inflammatory disorders of the heart, which are so frequently associated with rheumarthritis, as complications or as integral elements of the disease. Perhaps the latter is the more correct way of looking at them; for there can be no question that the heart is more often implicated in the course of rheumarthritis than many of the joints—especially the smaller joints; and the cardiac and articular affections owe their origin to the same cause. But inasmuch as we are obliged, in the present state of our knowledge, to hold fast to the anatomical point of view, and to regard the articular inflammation as the essential element in rheumarthritis, we must, to be consistent, regard all other organic disorders, however frequently they may occur, and however intimate their connection with the morbid process, as complications.

Foremost among them stands *myalgia*, that painful affection of the muscles known as "muscular rheumatism," and possibly dependent on inflammatory changes in their tissue. It is very commonly associated with rheumarthritis, and is not always limited to the muscles in relation with the inflamed joints, but may attack others at a distance from them. For a detailed description, the reader may refer to the section devoted to the rheumatic forms of myalgia.

Pericarditis and *endocarditis*, with which a certain degree of *myocarditis* is invariably associated, are of more importance. Authors vary widely in their statements about the frequency of heart-complications in rheumarthritis. For this there are many reasons. In the first place, they are not always to be easily recognized, and the diagnostic signs of their presence are of unequal value; so that where one physician may confidently assert their existence, another may hold his opinion in reserve. We all know, for instance, that a systolic murmur over the precordial region was enough, in Bouillaud's mind, to prove the existence of endocarditis. Secondly, there can be no doubt that great differences in this respect exist between cases occurring in different places, and more especially at different times; differences which oblige us to assume the existence of a *genius epidemicus* and *endemicus*. Again, it must not be forgotten that our statistics are, for the most part, based on hospital experience; and we know that, for various reasons, the different ages of man's life are very unequally represented in such institutions. Now, it is an undoubted fact, though one which has not received the attention it deserves, that heart-complications in polyarthritis are very much more common in young than in older patients; nay, it may be laid down as a law, that the younger the patient the greater the risk of his heart becoming affected. The risk is greatest before puberty; indeed, combining my own observations with those of others, I conclude that the heart is implicated in fully one-third of all the cases of polyarthritis occurring during this period. Vernay's statistics are even more unfavorable; he found that of twenty-two cases between the ages of fourteen and twenty, one only escaped endocarditis. The risk continues great till about the twenty-fifth year of life; after that age endocardial complications are the exception, save in cases where organic mischief has been left as a result of previous attacks of polyarthritis, such mischief always carrying a predisposition to renewed inflammatory changes with it. Again, treatment, as I shall have occasion to point out, seems to exert a decided influence on the liability to cardiac complications.

If, instead of inquiring into the frequency of heart-disease generally, we endeavor to distinguish between pericarditis and endocarditis, we find very little agreement among the data on record. This must be attributed partly to the causes referred to above, partly to the frequency with which the two forms of heart-mischief coexist or succeed each other in the same patient.

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Finally, the risk of cardiac complications appears to be greater among hospital patients than in private practice.

Bouillaud, who, as I have already mentioned, was very free with his diagnosis of endocarditis, found cardiac inflammation in 64 out of 74 severe cases of polyarthritis, and in only one out of 40 mild cases. Budd met with it in 21 out of 43 cases (48.8 per cent.); Fuller in 7 out of 39 (17.9 per cent.); Wunderlich in 26.3 per cent.; J. Vogel, of Giessen, in barely 50 per cent.; Lebert in 23.6 per cent. (pericarditis in 6.4 per cent., endocarditis in 2.9 per cent., both together in 14.3 per cent.). Bamberger[1] noticed pericarditis in about 14 per cent., and endocarditis in, at most, 20 per cent. Roth gives 18.8 per cent. for acute inflammatory affections of the heart; Ormerod, for pericarditis alone, 37.3 per cent., and Ball 20 per cent. Chambers found the heart implicated in 14 out of 200 cases (7 per cent.); 174 of these cases, treated with bicarbonate of soda, yielded 9 (5.2 per cent.). Dickinson, at St. George's Hospital, found the heart affected in 36 out of 161 cases (22.4 per cent.); 48 of these were treated with alkalies, and among them only a single instance of cardiac mischief occurred; of the remaining 113, the heart was implicated in 35 (39 per cent.). Among my own 56 patients (all private ones), cardiac complications occurred in 6 (10.7 per cent.); 2 had pericarditis; 1, endocarditis; 3, both at once. The ratio is much less favorable among the cases admitted into the Charité Hospital. Among 35 cases in the wards of Prof. Frerichs, Aug. Mayer met with pericarditis 7 times, with endocarditis once, with endopericarditis 4 times (total, 34.3 per cent.).

Many physicians have thought that the danger of heart-disease is greatest when a considerable number of joints is affected; this does not seem to be quite true, unless by "a considerable number" we understand any number above four. So also the assertion made by Reeves,[2] that pericarditis is most common when the upper limbs are affected, is in need of confirmation.

The symptoms to which these complications give rise differ in no way from those usual under other circumstances. But we may easily be led into the belief that they exist when they are really absent. As regards endocarditis, more particularly, prolonged and repeated examinations are often necessary before we can affirm it to be present. Inorganic or functional murmurs, very common in polyarthritis, are a fertile source of error; and the semblance of cardiac inflammation is further increased by pains in the pectoral and intercostal muscles, or in the diaphragm, with the feeling of oppression, the dyspnœa, and the acceleration of the pulse, with which they are associated. It is only when the development and progress of physical changes in the heart take place under the physician's own observation, that he is really entitled to affirm the existence of endocarditis.

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[1] Lehrbuch der Krankheiten des Herzens. Wien, 1857. p. 110 and 159.
[2] *Schmidt's* Jahrbücher, Band 161, S. 129.

Next in order of frequency to cardiac inflammation, though at a considerable interval, stand *pleurisy* and *pneumonia.* The latter is not very common; the former was noticed by Lebert in ten per cent. of his cases; it was most frequent on the left side, and often associated with pericarditis, from which it was doubtless propagated. Bilateral pleurisy, the two sides of the chest becoming affected in quick succession, has been repeatedly observed. As the symptoms of pleurisy are often obscure, those of a subjective kind—pain and dyspnœa—being referred to the joint affection and the attendant myalgia, while the physical examination of the chest can often be but imperfectly carried out, or may be altogether impracticable, the existence of pleurisy may very easily be overlooked. Like most of the exudations occurring in connection with polyarthritis, that into the pleural sac is commonly of a sero-fibrinous character and capable of being readily absorbed.

Inflammation of various mucous surfaces is by no means unusual. Foremost among these is *bronchitis* (noticed by Lebert in 9.3 per cent. of his cases; by A. Mayer in 5 out of 35 cases, two of which were chronic); then *pharyngitis* (noted in 7 of Lebert's, in 2 of Mayer's cases); lastly, *cystitis.* Lebert found the last-named disorder in two of his cases, and mentions that Faton (Thèse de Paris) has recorded several; for my own part, I have only met with it once as a complication of polyarthritis.

Among cerebral complications, *meningitis* has been observed with varying frequency in different localities and at different times. Cases may be found even in Stoerk (Ann. Med., II.), Stoll, Scudamore, etc. Among modern writers, Niemeyer alludes to meningitis; Lebert and Dowse[1] have each recorded one case. On the whole, however, this complication appears to be much less common in temperate than in hot climates, *e. g.*, in Turkey (Rigler, quoted by Hirsch). *Spinal meningitis* has also been referred to as a complication of rheumarthritis ; but the statements on the subject are not wholly trustworthy, partly because the tenderness and stiffness of the spine due to inflammation of the intervertebral joints or to implication of the dorsal muscles used often in former days to be attributed to meningitis ; partly because both the epidemic and the sporadic forms of spinal meningitis are very commonly ushered in by "rheumatoid" pains in the limbs, and the ailment is thus taken for a mere complication or metastasis of a rheumatic fever ; finally, because many cases of pyæmia with purulent meningitis have been mistaken for rheumarthritis.

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[1] Lancet, July 6, 1872.

In a fair proportion of cases the implication of the brain is notified by various psychical disturbances, which cannot be ascribed to the rapid rise of temperature, but take the form of true insanity, of "mental" disease in the narrower meaning of the term. They are provoked, or, at any rate, promoted, as Tuengel was the first to point out, by the pain and want of sleep. They exhibit every variety of excitement and depression, from well-marked mania to melancholia. Sometimes they last but a short time, and disappear without leaving any trace behind; sometimes they are protracted into the period of convalescence ; sometimes they may persist after complete recovery, when they constitute the "protracted form of rheumatic brain disease," which Griesinger was the first to recognize.

Again, rheumarthritis, like other febrile maladies, may determine an outbreak of delirium tremens in drunkards. When endocarditis exists, symptoms of cerebral disturbance may be caused by embolism of the arteries of the brain.

Other complications are met with from time to time, which stand in the relation rather of accidents than of incidents to the primary disease. Among them are *peritonitis*, *bed-sores*, *abscesses* (Lebert), and *intercostal neuralgia*. Moreover, some of the *eruptions* already referred to, and the *renal disorders* which are occasionally observed, may also be counted among the complications of rheumarthritis. Acute infective diseases are rarely associated with rheumarthritis. I have myself seen scarlet fever break out on the seventeenth day of illness, in a woman twenty-four years of age. The patient made a good recovery.

Course and Duration.

Even when uncomplicated, polyarthritis may exhibit many diversities in its course, depending chiefly on the behavior of the joints. When the articular inflammation is mild, and limited to a few joints, and complications are absent, the disease may terminate between the eighth and twelfth, or between the eighth and fourteenth days. This is the mildest form of the disease, whose character cannot always be foreseen from the outset, but only declares itself during the progress of the case by the abatement of the patient's sufferings and fever,—no fresh joints being attacked for several days,—and convalescence setting in. These milder forms frequently develop a graver character, fresh joints becoming involved before those previously affected have had time to recover. As a general rule, indeed, a severe attack of rheumarthritis is merely an aggregate of milder ones,—a series of mild paroxysms occurring in close succession and overlapping one another. Hence the protracted course of a severe attack; hence, too, the alternate remission and exacerbation of the local symptoms, and, consequently, the utterly atypic oscillations presented by the disease as a whole, by the pyrexia, etc. The cause of the inflammation, whatever it may be, has usually exhausted its violence, in these graver forms of the disease, by the end of the third, or, at latest, of the fourth week. The process then culminates, and the next two or three weeks are taken up by the complete or partial reabsorption of the exuded matters. The acute stage of the malady is thus brought to a close in six or seven weeks, though some particular joint may possibly require a little longer time for its restoration, and complete recovery may be deferred till after the second month is at an end. We very seldom see a case in which so great a number of joints is attacked from the outset, or during the first few days, as to enable us to recognize it at once as belonging to the more serious class, independently of possible complications.

I need hardly say that the mild and the severe forms of rheumarthritis are connected with each other by a vast number of intermediate varieties, which shade off almost imperceptibly into one another. As an approximative standard of severity, the number of joints affected throughout the attack may be taken, instead of that usually chosen—the duration of the illness; indeed, the latter, as a rule, depends on the former. The adoption of this standard is further prompted by the way the disease picks out certain joints (knee, ankle), which are, in severe cases, invariably affected. We may call those cases mild in which three or four joints at most are inflamed, and this in a moderate degree, such cases lasting a little under or over a fortnight. When from four to seven joints are attacked, and the illness lasts from three to five weeks, the case may be viewed as one of medium severity. Lastly, a severe case would be one in which from eight to twelve or more joints are involved, and which lasts longer than six weeks.

Among 108 cases, Lebert found 10 that lasted from 5 to 15 days, 58 from 16 to 35 days, 32 from 36 to 55 days, and 8 lasting for a still longer period (up to 80 days). Such data throw no light on the relative frequency of the different forms, as only a small proportion of the mildest cases would be likely to gain admission into a hospital.

It is plain that the presence of complications may greatly modify the course of the disease. They may completely efface those variations in the intensity of the local symptoms and in the patient's general condition which are all but invariably exhibited by uncomplicated cases. Since the most common of those complications, always excepting myalgia (so-called "muscular rheumatism"), are in themselves severe, or even dangerous, their presence will naturally convert any form of polyarthritis into a serious malady; but the duration of the illness is not necessarily prolonged by them, since it is for the most part characteristic of the inflammatory affections associated with rheumarthritis, that they are capable of undergoing speedy resolution.

Previous disease, or other debilitating influences, such as profuse hemorrhage, parturition, etc., may retard the progress of convalescence, and so prolong the malady without, however, appreciably lengthening its acute stage. On the contrary, most of the cases in which rheumarthritis follows scarlet fever and dysentery seem to run a shorter course than usual; and Bouillaud's plan of treatment by repeated and copious venesection, which used formerly to be practised, did not prolong the disease. Indeed, if we are to believe the assertions of its advocates, it actually shortened it; but this is probably an exaggeration, like many of their statements.

Diagnosis.

There is no difficulty in recognizing acute rheumatic polyarthritis. The joint affection and the fever—the two characteristic features of the disease—can hardly be overlooked by even the most superficial observer. On the other hand, there are several other maladies associated with inflammation or neuralgic pains in the joints, which may easily be mistaken for rheumarthritis. Foremost among these is pyæmia, which has over and over again, especially in former years, been confounded with rheumarthritis. Our chief means of distinguishing between them lies in the discovery of some local suppuration antecedent to the articular malady in point of time. We cannot always do this, however; but, even in default of this sign, the rigors and the temperature variations, the occurrence of metastatic deposits in other organs, especially in the lungs, the profound constitutional disturbance, the disorders of the sensorium, the icterus—all of them phenomena which scarcely ever occur in rheumarthritis—will put us on the right track. Nevertheless, many diseases of a pyæmic nature, especially certain varieties of puerperal fever, in which the characteristic febrile symptoms and the phenomena localized in the generative organs are not well marked, may puzzle us a good deal at first. But our doubts are usually set at rest by the further course of the disease. What I have said about pyæmia is true also of glanders, which often presents symptoms of the same kind; the patient's history, his employment, the formation of abscesses in the muscles, of pustules and ulcers on the skin and the nasal mucous membrane, finally the onset of delirium and utter break-up of the system, must serve as distinguishing marks. It is not easy to mistake an attack of gout for one of rheumarthritis, if we bear in mind that the former usually sets in suddenly during the night, after prolonged gastric disturbance; and further that, at any rate in the beginning, a single joint, especially one of the toe-joints, is attacked—a joint usually spared and scarcely ever affected alone by rheumarthritis. Again, gout is prone to occur at a time of life when polyarthritis is uncommon; the periarticular tissues are more affected, the pain is far more severe, and other constitutional troubles are associated with it. When there is a history of previous attacks of gout, we are still less liable to an error of diagnosis. Traumatic arthritis is very unlikely to affect several joints at once or in succession; moreover, it is usually attended by signs of injury. Scrofulous arthritis may be distinguished by its chronic course, the presence of other signs of scrofula, the tendency to pus-formation, etc. The articular neuroses, to which attention has been directed by Brodie, Stromeyer, and especially by Esmarch, are absolutely apyretic, but may, nevertheless, suggest the possibility of mild polyarthritis. The absence of fever and of any palpable alteration in the painful joint, the limited character of the affection, the freedom from pain during sleep—when the affected limb may be made to assume any position desired, the constitution, and above all the mental state of the patient—who is usually of the female sex,—finally, the prolonged duration of the symptoms—will certainly enable us to arrive at a correct decision in the majority of cases. Certain forms of articular pain occurring in the anæmic, in the subjects of scurvy, purpura hæmorrhagica, and hæmophilia, are often purely neuralgic, unattended by any change or swelling in the joints; sometimes, however, these symptoms are present in a slight degree, and we may hesitate whether to include such cases under the head of rheumarthritis or not; for my own part, I think they ought to be kept separate, as they never pass into the graver forms of the disease, are never attended by the sweating that is so constant a feature of true rheumarthritis, and are never followed by its complications. In purpura, more particularly, we find painful swellings of the joints, usually confined to the lower limbs, and especially prone to show themselves in the feet. These swellings are not attended by fever, and are not always truly inflammatory; they are often due to disorders of the collateral circulation, provoked by embolism—which Bohn[1] believes to underlie many cases of purpura,—or they may be due to œdema resulting from those changes in the vascular walls or in the blood itself, to which, in other instances, we must attribute the causation of the hæmorrhages.[2]

Various forms of multiple inflammation about the joints are met with in infancy, and may simulate rheumarthritis. Such are *acute rickets*, *syphilitic osteochondritis*, *and separation of epiphyses* due to many other causes. The circumstance that these disorders are peculiar to an age which is all but exempt from rheumarthritis, is enough to distinguish them from the latter. Moreover, they all begin in the epiphyses, from which they may or may not spread to the articular cavity itself; finally, the patient's history and other symptoms will furnish us with a correct clue.

I have already pointed out that the diagnosis of complications—more especially of endocarditis—may prove difficult. Supposing heart-disease to have existed previously, it may be impossible, in the absence of evidence from the patient's history, to decide whether the endocardial mischief is of old standing or of recent origin. I have also mentioned that the implication of the intervertebral joints and the muscles of the back may simulate meningitis. The latter should never be assumed to exist without more positive evidence.

Issues and Sequelæ. Prognosis.

Rheumarthritis is not among the more dangerous diseases. Death is, upon the whole, rare; when it occurs, it is usually due rather to complications or unfavorable conditions of an individual kind than to the joint-affection, even when this is severe. Haygarth lost 7.1 of his 168 cases, Raymond[3] only 3.3 per cent. out of 490. The latter seems to be about the usual death-rate, for Lebert's mortality was only a little over 3 per cent., Roth's, 3.7 per cent. Of fifty-six patients under my own care, two died (3.6 per cent.) with cerebral symptoms and a sudden rise of temperature. It is in this way that death occurs in most of the fatal cases. I have already pointed out that the risk of death is greatest in persons of intemperate habits. In a smaller proportion of cases death is caused by complications while the polyarthritis is still present, most frequently by peri- or endocarditis; more rarely, by meningitis.

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[1] Jahrbuch f. Kinderheilkunde. N. F., S. 391.

[2] Cf. *Scheby-Buch*. loc. cit.

[3] See *J. Vogel*, loc. cit., p. 485.

In the non-fatal cases, which form a vast majority of the whole number, the ultimate issue depends mainly on the presence and nature of complications. Hence, there is no great difference in this respect between mild and severe cases. It is only in the very mildest—running their course with a sub-febrile temperature—that we are justified in giving a favorable prognosis. In all the rest the prognosis must be left doubtful for as long as the fever lasts, or, at any rate, till the third week is reached, after which date complications rarely arise. Now, as heart complications are the most serious of all in their ulterior consequences, and as they are most frequent in youth, so the chances of complete recovery are less promising in young patients than in adults, owing to the risk of permanent disease of the heart. This is not unfrequently followed by chorea, especially when the mitral is the affected valve. On the other hand, when rheumarthritis attacks a previously healthy person of twenty-five or thirty, it usually terminates in complete recovery without sequelæ; there remains, at most, a tendency to renewed attacks after a variable interval of time. In a relatively small number of cases, when the articular inflammation has been very intense or protracted, permanent alterations are left in one or more of the joints, *e. g.*, chronic inflammatory conditions, liable to exacerbation from trivial causes (Cf. Chronic Rheumatic Arthritis), thickening, ankylosis, or even ulceration. Such consequences are more common after repeated attacks, and especially after the subacute forms of rheumarthritis, or such as drag on for a length of time. Whether suppuration in a joint, leading to pyæmia, ever really happens, as described by older writers, seems to me extremely doubtful. Pyæmia was probably mistaken for rheumarthritis in such cases. Occasionally, however, rheumarthritis *may* issue in pyæmia; but the immediate cause of the latter is then an ulcerative endocarditis.

The presence of old heart-mischief always makes the prognosis a grave one, even when the patient is well up in years, for an attack of rheumarthritis is almost certain to aggravate the organic disease.

Mental disease, mostly taking the form of melancholia, is more common as a sequela in adults than in children. The prognosis is, upon the whole, a favorable one. It does not usually start as an independent sequela, but grows out of the psychical disturbances previously alluded to as occurring during the fever.

Finally, Duffey refers to orchitis as a common sequela of rheumarthritis at Malta. It usually ends favorably.

Treatment.

The prevention of rheumatic polyarthritis demands the same precautions as the prevention of any of the other results of "chill." These precautions are: to avoid all sudden and violent changes of temperature; to wear woollen clothing next the skin; to harden the system. These rules should be followed with especial strictness by those predisposed to rheumarthritis, either by the nature of their employment or by having undergone a previous attack. The advice given by Eisenmann for avoiding the "rheumatoses" (affections caused by chill) should be laid to heart, viz., to continue the exercise by which the body was heated just before exposure to cold or wet, and to defer repose until a complete change of garments has been effected. This advice is usually followed, on the promptings of personal experience, by those who are much exposed to the weather while engaged in active exercise. Another precaution, specially recommended by hydropathists, is energetic friction of the skin. It is assuredly impossible to prove that in any given case a "chill-disease," and especially an attack of rheumarthritis, has been prevented by one or other of the measures just alluded to. But the same uncertainty clings to nearly all our methods of prevention. We do know, however, that the operation of those measures is diametrically opposed to certain of the consequences due to chill. Continued muscular exertion, and the development of heat which it entails, supply the losses due to refrigeration of the surface, and promote that flow of blood and juices to the periphery, that "turgor" of the skin and muscles, which the chilling process threatens to arrest. Friction of the skin has the same effect, and serves, moreover, to stimulate the cutaneous nerves; the precise effect of their stimulation, however, we do not at present understand. But then we are just as ignorant of the exact mechanism of the process whereby a chill produces disease. We cannot but admit that it exerts some influence upon the heat of the body and upon the circulation; and this is enough to justify us in adopting the recommendations made above.

As regards the actual treatment of polyarthritis, it has varied with our theories concerning its pathology; at any rate, since rational therapeutics—*i. e.*, methods of treatment either really or apparently in harmony with accepted views on pathology—were substituted for traditional empiricism.

A strictly expectant method has never been able to hold its ground for any time in the face of the manifold disturbances and dangerous complications urgently calling for interference. A series of cases, treated on the expectant plan, impressed Lebert with the belief that the disease was more protracted, and attended by graver complications when left to itself than when subjected to treatment. The strictly antiphlogistic method, as it used to be understood,—bleeding, refrigerant salines, mercurial and antimonial preparations,—has also proved inadequate. Experience has shown that these measures, whether singly or in combination, exert no influence whatever on the progress of the disease.

They may afford temporary relief from particular symptoms; but such relief is dearly bought at the expense of various disadvantages, nay, even of serious damage to the system. This is especially true of blood-letting, both of the moderate venesection practised ever since the days of Sydenham, and still more of the extravagant bloodshed of which Bouillaud and his followers (Pelletan, Raciborski, and others) were guilty. It is likewise true of the large doses of nitre recommended by Brockley and Macbride in the last century, by Gendrin, Martin Solon, Basham, and others in this; of tartar emetic, calomel, corrosive sublimate, etc. Every one of these remedies is capable, upon occasion, of subduing the fever more or less effectually ; but this action, uncertain as it is, forms no equivalent for the attendant troubles—the gastro-intestinal irritation, the diarrhœa, nausea, and vomiting (troubles doubly annoying to a patient whose every movement causes agony), the risk of fatal collapse, etc.

The belief in a specific cause of rheumarthritis has led to the perpetual renewal of attempts to discover a specific remedy. Even at the present day we find a number of remedies which claim to be regarded as specifics, their claims resting on the different theories concerning the nature of the *materies morbi*, and the best way of rendering it harmless or of removing it altogether from the system. Such attempts are quite legitimate ; but no remedy has, up to the present time, established its claim to universal favor; none has been discovered to possess undoubtedly specific virtues, to be capable of summarily arresting the disease under all circumstances.[1] Each individual remedy is lauded for some special property : one is believed to shorten the attack, another to subdue the pain and fever, a third to ward off dangerous complications. The natural course of the malady is so irregular that it is no easy matter to decide on the value of any particular mode of treatment; and the difficulty is enhanced by the limitation of the clinical material at the disposal of the individual observer. Rheumarthritis affects but a small fraction of the cases admitted even into a large hospital, and many years are required for the collection of a series of cases large enough for statistical treatment. This involves the interference of collateral influences, such as, *e. g.*, that of the *genius epidemicus*, for which no exact allowance can be made. Hence, I shall not attempt to do more than enumerate those remedies and methods which have been tried by reliable observers, and recommended by them on the ground of a tolerably large clinical experience.

Lemon-juice, originally recommended by Dalrymple and Rees, found by Fuller to be inoperative, by Inman,[2] on the other hand, to be highly curative, has been methodically tried by Lebert. Beginning with four ounces a day, he increased the daily allowance by one ounce every day during the first few days of the disease till six ounces had been reached; this quantity was given in twelve doses (a tablespoonful of the juice every two hours in half a glass of sugared water). This mild and pleasant remedy was found, on the whole, to mitigate the fever and shorten the average duration of the disease. In thirty-six cases treated on this plan the illness lasted, on an average, 28.4 days, while in fifty-seven cases treated otherwise, the average duration was 34.7 days. The risk of complications was not lessened, or only lessened by the abbreviation of the malady and of its more severe symptoms. Gull and Sutton also found that the acute stage was brought down to 6.8 days by the lemon-juice treatment, and to 6.75 days by alkalies; while it lasted 8.4 days under blistering, and 9.1 days under a purely expectant regimen.

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[1] For the use of salicylic acid in acute rheumatic polyarthritis, see the Translator's Note at the end of the volume.

[2] British Med. Journal, 24 October, 1857.

Authors have occasionally recommended *alkalies*, from an early period, on theoretical grounds, viz., in order to antagonize the abnormal production of acid supposed to go on during rheumarthritis. But it is only of late years that the alkaline treatment has been thoroughly tested. The results of the investigation, principally conducted by English physicians, are decidedly favorable, the frequency of cardiac complications having apparently been diminished by this plan of treatment. Thus, Furnivall treated about fifty cases with alkalies without the heart being implicated in any one of them. Chambers found the heart affected in nine only out of 174 cases treated with large doses of bicarbonate of soda, while it was affected in five out of 26 cases treated in other ways. Dickinson had one case of heart-disease among 48 patients treated with alkalies, and 35 cases among 113 patients treated otherwise. Fuller found heart-disease developed, during the alkaline treatment, in nine only out of 417 cases. Moreover, this method appears to exert a favorable influence on the duration of the malady as a whole, Gull and Sutton giving 13.5 days as the total length of the disease under alkalies, 15.7–19 days when otherwise treated; the cases left entirely without interference lasting longer than any of the rest. Kersten, too, observed that rheumarthritis ran a shorter and milder course under the influence of alkalies. I myself treated 34 of my 56 patients with large doses of bicarbonate of soda, with only two instances of heart complication; while among the remaining 22 cases subjected to various other methods (nitrate of soda, quinine, colchicum, digitalis) the heart was implicated four times. These figures are enough to stimulate us to further inquiry; for if we prevent cardiac mischief we all but abolish the immediate risk to life, and minimize yet more effectually the ulterior danger of permanent organic disease. The fact already alluded to—that patients under twenty-five are peculiarly liable to cardiac complications—must of course be allowed for in any future comparisons between the results attained under different methods of treatment.

Whether the beneficial effects of alkalies be really due to their neutralizing an excess of acid in the system must of course continue doubtful so long as the very existence of such excess of acid is a mere hypothesis. Even were its existence proved, the nature of its connection with the heart-mischief would remain to be determined. We might continue to suppose that the introduction of the carbonates or vegetable salts of the alkalies in large quantities might lessen the tendency of the blood to coagulate, and thereby lessen the chance of fibrin being deposited on the valves. It is interesting to note that inhalations of carbonate of soda have been employed with excellent effect by Gerhardt[1] in recent endocarditis.

Since no effect can be expected from alkalies unless they are given in very large doses, we must choose sodic salts in preference to the corresponding potassium or ammonium compounds. The former base is, in itself, indifferent; the latter may do harm to the heart and the nerve-centres. Sodic salts are preferable to magnesia likewise; the latter was much employed by Schoenlein, and may of course be occasionally resorted to by ourselves when there is obstinate constipation. The best plan is to give from five to ten drachms a day of the bicarbonate, acetate, tartrate, or citrate of soda in sugared water, until the urine becomes neutral or feebly alkaline, as it usually does on the second or third day after the treatment has been begun, increasing simultaneously in amount. The daily dose should then be reduced, and only increased whenever the urine shows a tendency to become acid. This plan is followed by no ill effects; sometimes there may be a little diarrhœa, but this always subsides when the dose is lessened, and may always be prevented by adding a few drops of laudanum to it. It is possible that the remedial effect might be attained more speedily by employing Gerhardt's inhalations of carbonate of soda; but on this point I cannot speak from experience. I am equally unfamiliar with the use of the carbonate of lithia, and the compounds of this metal with the vegetable acids; they may fairly be credited with properties similar to those of the corresponding salts of potash and soda.

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[1] Lehrbuch der Kinderkrankh. 1874. p. 237.

This is the place for saying something about *trimethylamine* (often confounded with its isomer, *propylamine*). Its powerful basic properties connect it with the alkalies, even though it may differ from them in its physiological action. Awenarius,[1] who was the first to give it in rheumarthritis and the other forms of rheumatic disease, ascribes to it a singular power in removing pain and swelling from the joints. He orders twenty-four drops of the remedy in six ounces of water, sweetened and flavored with peppermint, a tablespoonful of the mixture to be taken every two hours. He believes himself to have frequently seen all the symptoms of the disease vanish after twelve doses had been taken. Von Bursy,[2] in Mitau, found the remedy very effective for a time; but it seemed, afterwards, to lose its efficacy. Lebert found it useless. Recently, however, Coze[3] and others, especially Dujardin-Beaumetz,[4] have again referred to it in glowing terms, on the ground of a fairly extensive series of observations, as capable of quickly controlling the pain and fever,—and of subsequently removing the articular swelling also. They found the secretion of urea lessened during its administration. The data at our disposal are still, however, quite inadequate to

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[1] Mediz. Zeitung Russlands, 1858, No. 6.

[2] Ibid., 1859, No. 29.

[3] *Fargier-Lagrange*, Essais thérapeutiques sur la trimethylamine. Strasbourg, 1871.

[4] Union Médicale, 1873, 6 and 7. Gazette hebdomad. 1873, No. 13, seqq.

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allow of our forming a conclusive judgment as to the value either of the uncombined trimethylamine, or of its hydrochlorate, which has been preferred on account of its greater purity.

As regards the action of *colchicum*, the evidence is very contradictory. While some regard it as the one specific and infallible "antirheumatic," and even employ it as a means of determining whether a particular disease be "rheumatic" or not (Eisenmann), others reject it as absolutely useless. Even the champions of the remedy, however, are not agreed upon its mode of action: whether it be curative in purgative doses only, or whether its irritant effect on the bowels should not rather be avoided; whether it be more efficacious in acute cases, when the fever is at its height, or in chronic cases unattended by fever. Impartial observation fails to confirm any of the striking results that used to be recorded, whatever be the preparation employed (tincture, wine, or extract of the seeds). Even the opiated tincture of colchicum (six parts of tincture of colchicum to one of laudanum, eighteen to twenty or more drops to be taken three or four times a day), recommended by Eisenmann for all the divers forms of "nervous and vascular rheuma," often fails completely—at any rate, in acute polyarthritis, when the malady is at its height,—or acts very slowly, perhaps no better than the opiate would act by itself. But we must not rush into the opposite extreme of denying all virtue to colchicum. A considerable number of cases have been put on record in which the disease has been checked after several days' use of the remedy. It may be that the differences in its action depend upon the employment of different preparations. *Colchicin*, certainly the most active constituent of the plant, should therefore be employed when possible. Skoda[1] speaks highly of its beneficial influence upon the inflammatory changes in the joints; he prescribes one grain of colchicin in from two to three drachms of water, with a few drops of rectified spirit to assist in dissolving it; five drops of this solution are to be taken twice or three times a day, until (usually in two or three days) active purging sets in and the pains abate.

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[1] Wien. Mediz. Presse, 1866, No. 6.

Aconite and *veratria* have repeatedly been substituted for colchicum, but they have never met with much favor. Their influence on the inflammation and pain in the joints is not to be depended on; their antipyretic action, on the other hand (especially that of veratria), is unquestionable; but as the fever in rheumarthritis does not often rise to a dangerous height, and when it does, may be combated by means that are at once more effectual and less dangerous, the employment of aconite and veratria offers no special advantages.

Finally, we must consider—among specific remedies—the *blister treatment* advocated by Legroux, Dechilly, and above all, by Davies. The last-named author directs us to surround every one of the affected joints with a strip of blistering plaster, and promises that within twenty-four hours, as soon as the blisters have risen and their contents have been evacuated, the good effects will be manifest, the pain and fever will subside, and the urine will be neutral or even alkaline. The duration of the disease, as a whole, is said to be shortened, cardiac complications are prevented, or actually removed when they already exist. Davies explains these results by supposing the blistering to eliminate a *materies morbi*—possibly lactic acid—from the system. Other observers are by no means agreed on the subject. I have myself repeatedly seen the blister-treatment carried out in the wards of the Berlin Charité,—without any result beyond a slight—and often only temporary—diminution of the articular swelling, and a transient fall of temperature resembling that produced both in sick and healthy persons by extensive irritation of the skin. I never saw the blistering cause any change in the state of the urine, and the other effects were not more brilliant than those produced by other modes of treatment. Again, the simultaneous application of a number of blisters is not without its drawbacks; strangury is no very uncommon result of the absorption of cantharidin, and the urinary irritation may even be intense enough to culminate in a fibrinous inflammation; weakly and sensitive patients, moreover, complain bitterly of the burning pain caused by the blister at its point of application. We may add that Davies himself regards the administration of alkalies as a desirable addition to his blister-treatment; and some part of the effect, so far at least as the reaction of the urine is concerned, and the rarity of cardiac complications, may possibly be due to the former element.

What is the conclusion to be drawn from a consideration of all the above facts? That no one plan of treatment is capable of arresting rheumarthritis; that none among them has been certainly proved even to exert an influence on the chief symptom of the disease, viz., the joint affection. The most that we can say is that certain remedies tend to shorten the malady and to lessen the tendency to cardiac complications. Now, as the danger to life is, in most cases, solely dependent on this tendency, it is clear that to diminish it must always be a main object of our endeavors, and one to which almost all other indications must give place. Hence, I recommend the methodical administration of alkalies in every case; their efficacy in averting heart-disease has been repeatedly shown; they give rise to no collateral effects of an injurious kind, and they are compatible with other remedies and modes of treatment regarded as specific. In young patients especially, and while the fever persists, alkalies in the largest possible doses should be energetically employed. At a more advanced time of life, they may be omitted with less danger, and replaced by alkaline beverages, soda and seltzer water, and the methodical administration of lemon-juice, which seems often to shorten the duration of the disease.

In this, as in every other malady which may run a favorable course without medical interference, it is the first duty of the physician to ward off disturbing influences; and, secondly, to combat such symptoms as are especially disturbing or dangerous. Even in the mildest cases, the patient should be kept in bed and in as easy a position as possible; the temperature of his room should be moderate, his coverings light,—since heavy blankets are painful to the inflamed joints and increase the sweating unnecessarily. For this reason, and also to spare the patient every painful movement, it is important, when the case is at all severe, to substitute a mattress or a water-bed filled with tepid water for the usual feather-bed, which requires to be made too frequently. The patient's diet need not be so much restricted as in other highly febrile disorders; it is enough to prohibit heavy flatulent food, and in other respects to consult the patient's own appetite. To relieve thirst, I recommend the alkaline waters already alluded to, instead of the acidulous drinks and lemonades usually given. Patients in the habit of taking stimulants should not be entirely deprived of them. As regards special symptoms, the fever does not usually require interference ; it is only in those rare and ill-omened cases in which the temperature runs up to a dangerous height, that we must strive at any cost to lower it. We have recourse for this purpose to cold baths repeated every few hours, and especially to cold affusion ; these measures, it is true, only reduce the temperature for a time, and alleviate the brain symptoms ; occasionally, however, they have been known to overcome the danger altogether. Large doses of quinine, given by the mouth, or subcutaneously (the amorphous hydrochlorate is preferable to all other preparations of the alkaloid), may be used to supplement the action of the baths, when there is time for them to operate. The alarming signs of collapse which are usually present call for the administration of powerful stimulants, especially of such as can rouse the action of the heart, viz., camphor, musk, strong wines, brandy, etc. In less urgent cases, unaccompanied by severe brain symptoms, where acute inflammation of the joints coexists with an evening temperature above 39° C. (102.2° F.) or 39.5° C. (103.1° F.), quinine, in doses of from fifteen to thirty grains, given towards evening, is sufficient of itself to moderate the violence of the disease. Other specific virtues which used formerly to be attributed to quinine are purely imaginary ; when given in large doses, it may cause slight stupefaction and a sort of narcosis. In vigorous individuals, when the heart's action is so greatly excited as to lead to the suspicion of a threatening endocarditis, digitalis in large doses may be advantageously prescribed.

The attention of the physician is largely claimed by the articular inflammation and its attendant pain. Some relief may be afforded by raising the affected limb and putting it in such a position as to reduce the afflux of blood, and to relax the tendons and ligaments to their utmost. As regards other local measures, the utmost difference of opinion prevails. The joint-affection is looked at by many authorities in the light of a *noli* *me tangere;* they try to shield it from all contact, even from the air, for fear of evil consequences, such as driving in the inflammation upon internal organs. Hence the custom, prevalent to this day, of wrapping the inflamed joints in cotton-wool, dry or greased, in flannel, oiled silk, etc., and avoiding all interference, except lubrication of the joints with oily matters, while guarding them carefully against cold and damp. Now, these warm coverings are not only useless, they actually tend to aggravate the feeling of heat and other inflammatory symptoms. The fear of causing disease of internal organs by vigorous attempts to reduce the local inflammation, is certainly exaggerated. Cold, in the form of wet compresses, and, still better, of ice-bags (Stromeyer, Esmarch[1]), is not only harmless, but has repeatedly been proved to be beneficial in lessening the duration of the inflammatory process in the joint; nay, even the energetic employment of hydropathy has been followed by good results.[2] We are still in want of more extensive information concerning the effects of ice—preferred by Esmarch to cold-water compresses, because the latter soon become warm and have to be changed, exposing the patient to the risk of a chill. Other antiphlogistic measures, such as local blood-letting by leeches, mercurial inunction, etc., may for the most part be dispensed with; they cannot do much good, while their extension to a number of joints is not unlikely to be injurious. They are the less needful, as the swelling of any particular joint usually subsides of itself in a few days.

We have still to consider a series of more or less effectual, and wholly innocent, remedies for the relief of pain and of the joint-affection in its entirety. Their employment must be regulated by the severity of the symptoms, by the circumstances peculiar to each case, and by external conditions. Injections of carbolic acid (one Pravaz syringe filled with a one per cent. watery solution) under the skin covering the affected joints, as recommended by Kunze,[3] are at once convenient and safe. I have myself employed them in two cases, and was struck with the very rapid way in which they relieved the pain. Their action is far more certain than that of ethylene chloride (Dutch liquid) or of ether (the former recommended by Wunderlich, the latter by Niemeyer) rubbed into the affected joints, or even of the narcotic unguents which used formerly to be prescribed. Painting the joint with carbolic oil (one part of the acid in fifteen of linseed oil), as recommended by Hruschka and Betz, is worth a trial, though it is certainly inferior to hypodermic injection. Fixation of the affected joints by starch or plaster-of-Paris bandages has recently been proved to be of great use. This method was originally suggested by Varlez,[1] Forget,[2] Seutin, and Gottschalk; it has recently been advocated afresh by Concato, Heubner,[3] and Oehme. The last-named author has shown by comparative trials that the duration of the articular affection and the attendant fever, as well as that of the disease as a whole, may be shortened; further, that the fixation of an inflamed joint actually exerts a beneficial influence of a preventive kind on neighboring joints. Inasmuch, however, as the method in question, with all its advantages, is rather hard to carry out, its adoption must be limited to such cases as have failed to obtain relief from measures of a simpler kind.

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[1] Verhandlung d. Berlin. med. Gesellschaft. Sitzung v. 29 März, 1871.

[2] *S. Bonsaing*, Wiener med. Presse, 1868, No. 38.

[3] Deutsche Zeitschrift f. pract. Medizin, 1874, No. 11.

The sleeplessness usually depends upon the pain in the joints, and the two symptoms disappear together. When our treatment of the joints fails in procuring sleep, a hypodermic injection of morphia or a sleeping-draught may be given at night (morphia, opium, chloral hydrate, bromide of potassium). I have found morphia with chloral hydrate (muriate of morphia, one grain; chloral, eight scruples; water, syrup, of each one and a half fluid ounces—one or two tablespoonfuls to be taken at bedtime) very effectual in cases of rheumarthritis. I make it a rule never to give Dover's powder; its diaphoretic action is undesirable.

To relieve the excessive sweating, sponging with vinegar and water used at one time to be recommended. When the "acid" theory came up, an extremely dilute solution of potash was employed instead; the latter, however, is not primarily intended for the relief of the perspiration; it is effectual when cold, but then it exposes the patient to the risk of being chilled. Hence, the administration of acetate of lead (Ph. Munk) or of atropia (Fraentzel) should be preferred.[1] I have seen good results from the latter alkaloid given in doses of from one-sixtieth to one-thirtieth of a grain *per diem;* it is wiser to administer it every other day, or even at longer intervals, as it soon loses its power when continuously employed.

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[1] Arch. générales. XIV. 1827.

[2] Bulletin gén. de Thérapeutique, 1848, Juin.

[3] Archiv der Heilkunde, 1871, XII., 341.

The treatment of rheumarthritis, apart from the *régime* and dietetic rules prescribed above, may be briefly summarized as follows: In every case, so long as there is fever, the patient should take the bicarbonate or some vegetable salt of soda in the doses indicated above; with this we may by all means combine colchicin or tincture of colchicum, if we believe this remedy to possess a specific action; tincture of opium may also be added if the state of the bowels appear to require it. In mild cases, when the tenderness and swelling are inconsiderable, the joints should be covered with a light linen sheet, and supported on a leather cushion or stuffed pillow, or else immovably fixed in a suitable position on a light splint made of pasteboard or thin wood. When the pain is more severe, we may try the effect of carbolic acid rubbed into, or, still better, injected under the skin covering the most acutely inflamed joints. If there be much restlessness, the mixture of morphia and chloral may be given at night. Should these measures prove insufficient, I recommend the application of ice-bags, as practised by Stromeyer and Esmarch, when the inflammatory symptoms are very violent; should they be alarming or disagreeable to the patient, we may try to support the joints by more solid apparatus of pasteboard or plaster-of-Paris. Trimethylamine may also be allowed a trial in such cases. When the intervertebral joints are implicated and there is much pain in the muscles of the back (a region to which the above measures are inapplicable), we may find ourselves obliged to resort to local blood-letting by leeches or cupping, and—with an especial view to the alleviation of the patient's agony—to the subcutaneous injection of morphia.

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[1] Centralblatt f. d. medic. Wissensch. 1866. p. 545. Also Virchow's Archiv, LVIII. 120.

Particular symptoms, when very prominent, such as fever, collapse, sweating, must be combated by the special measures described above. Occasional paroxysms of dyspnœa and palpitation commonly yield to a mustard poultice over the præcordia, in conjunction with nervine stimulants (tincture of valerian, from fifteen to twenty drops every fifteen or thirty minutes).

When the inflammation is slow to abandon a particular joint, the latter remaining swollen after the fever has completely subsided, we may endeavor to promote absorption by leeching and mercurial inunctions, by blisters, by external applications of iodine (either in the form of an ointment or in that of the tincture), or by warm poultices or wet compresses, regulating our choice by the stage of the inflammatory process. In such cases the internal administration of iodide of potassium, with which many physicians combine colchicum, is likewise indicated.

Such brain symptoms as are not ushered in by a rapid elevation of temperature need no special treatment while the disease is at its height; should the restlessness and excitement be very great, a large dose of chloral and morphia may be given.

Complications and sequelæ must be treated on the principles peculiar to the affected organ. To guard against the occurrence of chronic rheumatic arthritis (the so-called "chronic articular rheumatism") the convalescent must be warned against over-exerting those joints which were inflamed, and exposing himself to cold and damp. To prevent a fresh attack, the patient must be urged to adopt the preventive measures which have already been enumerated.

Appendix.

Gonorrhœal Arthritis (Arthromeningitis gonorrhoica).

LITERATURE.—*W. Musgrave*, de Arthritide anomala. Oxford. 1707. Cap. II.—*Swediaur*, von der Lustseuche. Berlin. 1803. I.—*Holscher*, Hannoversche Annalen, 1844. IV. and Schmidt's Jahrb. XLV. S. 47.—*Potain*, Schmidt's Jahrb. LXX. S. 320.—*Brandes*, Archives génér. 1854. II. September.—*Rollet*, Annuaire de la

syphilis. 1858. p. 2. Schmidt's Jahrb. CIV. S. 175.—*Olioli*, Ann. universali, 1858; Schmidt's Jahrb. CIV. S. 175.—*Oppolzer*, Allgem. Wien. med. Ztung. 1859. 2.—*Duncalfe*, Schmidt's Jahrb. CXVIII. S. 40.—*Elliotson*, ibidem.—*Sigmund*, Wien. med. Ztung. 1858. No. 36.—*Peter*, Union méd. 1866. No. 141.—*Fournier*, ibidem, No. 145. Discussion des soc. méd. des hôpitaux.—*Greenough*, Boston med. and surg. journal, 1867, December. Jahresber. von Virchow und Hirsch. 1867. II.—*Voelker*, de l'arthrite blénorrhagique. Paris. 1868.—*Nunn*, Lancet, 1871. II. No. 26.—*Bond*, ibidem, 1872. I. No. 11. See also special treatises on venereal diseases.

Etiology.

During an attack of gonorrhœa an articular inflammation occasionally sets in, which, owing to its similarity to rheumatic affections of the joints, is also known as gonorrhœal or urethral rheumatism (*Trippergicht*—gonorrhœal gout).

The disease is much more common in the male than in the female sex, and has been almost exclusively observed, for obvious reasons, between the age of puberty and that of forty or fifty. Cold, damp, and atmospheric causes generally exert no influence on its production. Persons attacked by gonorrhœal arthritis are mostly free from any history of previous rheumatic affections of the joints. The disease almost always makes its appearance at a relatively late stage of the gonorrhœa—when this has lasted for at least one week, or when there is a persistent gleety discharge. It is not uncommon to see the same person attacked again and again, every time he contracts a gonorrhœa.

The connection of this form of arthritis with the urethral inflammation used formerly to be explained by supposing the gonorrhœal virus to undergo a sort of metastasis. Nowadays, we either assume an infective process to set out from the diseased mucous surface, or we regard the joint-affection as a reflex phenomenon; the latter view receiving support from recorded cases in which articular inflammation has been seen to follow other varieties of urethral irritation (*e. g.*, catheterism). But such cases are extremely rare; the true nature of the articular inflammation is sometimes open to question, at other times of an unquestionably pyæmic character. Moreover, were the reflex hypothesis correct, gonorrhœal arthritis should occur by preference in the recent and painful stages of urethritis. Finally, the very possibility of inflammation being set up by reflex irritation is, as a general proposition, far from established. The most probable view is that the inflammatory irritation is gradually propagated from the urethra to the sacral plexus and the spinal cord, where it affects trophic nerve-fibres. Gonorrhœal arthritis would thus be assimilated to those articular disorders which occur in many diseases of the spinal marrow, and possibly to many cases of arthritis deformans likewise (cf. the chapter on this disease). On this view, indeed, the presence of the specific gonorrhœal virus would not be necessary; but as this virus is the most common cause of urethral inflammation, and as it may possibly be endowed with a greater power of propagating the inflammatory process than is possessed by other irritants, we may account for the fact that the form of arthritis now in question is usually associated with the specific form of urethritis.

The comparative rarity of the disease in women may possibly be due to the circumstance that their vaginal and urethral mucous membranes (either of which may be affected by gonorrhœal inflammation) are thicker and more tough than the lining of the male urethra.

Symptoms.

The inflammation is commonly situated in one knee-joint; it is less usual to find both affected. The left knee seems to be more often attacked than the right one; out of five cases under my own observation, the left knee alone was attacked in four, both knees together in the fifth. It is very unusual to find the ankle-joints implicated likewise; the temporo-maxillary joint is said to have been affected in some cases. But there can be no question that many cases, in which several joints became successively inflamed during an attack of gonorrhœa, were simply cases of rheumarthritis accidentally associated with the urethral malady. This explanation of the facts is corroborated by a consideration of the attendant phenomena in each case.

The inflammation usually runs a subacute course and causes an abundant serous or sero-fibrinous exudation, which does not appear to differ in any respect from other inflammatory effusions into the joints, though Méhu found it (in a single case) to contain mucin, an ingredient said to be absent from the articular contents in rheumarthritis. In harmony with the subacute course of the disease, the pain is much less severe, the heat and redness of the skin much less marked, than in acute polyarthritis. Fever is only present at the outset, and is never severe; on the other hand, the knee is usually much swollen, and fluctuation is distinct. The abundant sweating, the inflammation of serous membranes, and especially of the heart, which are so characteristic of rheumarthritis, are not observed in the gonorrhœal affection of the joints. Moreover, the articular inflammation shows no tendency to shift its position or to disappear suddenly; on the contrary, it usually drags on for several weeks; months may even elapse before the exudation is entirely absorbed. The risk of its passing into chronic dropsy of the joint is much greater than in rheumarthritis. Otherwise, gonorrhœal arthritis is unattended by danger.

The statements made by older authors, to the effect that the joint-affection might disappear simultaneously with an exacerbation of the urethral discharge, are based either upon a fallacy of observation or upon an accidental coincidence. The same is true of the belief that the articular inflammation is caused or preceded by a "retrocession" of the discharge. The absence of the characteristic symptoms of rheumarthritis, the localization of the disease in the knee-joint, and its more sluggish course, are sufficient of themselves to make us suspect the presence of a gonorrhœa, which ought always to be inquired for in such cases. Should the existence of a discharge be ascertained, and no other cause be found, the inflammation must be regarded as gonorrhœal.

Treatment.

This is purely local, and should be directed as soon as possible to the removal of effusion. It is indispensable in all cases that the patient should keep the affected limb or limbs at rest, and, if possible, somewhat raised. The inflammatory symptoms must then be combated, in proportion to their intensity, by local bleeding, cold, inunction of mercurial or iodine ointment, painting with tincture of iodine, blisters, and, when absorption is delayed, by the early application of pressure.

An attempt may, at the same time, be made to cure the urethral discharge; but it is advisable to avoid the use of irritating and painful injections, as they may contribute to the extension of the inflammatory irritation.

II.—Arthritis Rheumatica Chronica.

(Chronic Rheumatic Arthritis.)

LITERATURE.—Consult the works referred to under the remarks on Rheumatic Affections in General, Acute Polyarthritis, and Arthritis Deformans.

Etiology.

Chronic rheumatic arthritis (chronic articular rheumatism, polyarthritis synovialis chronica, [Hueter] rheumatismus articulorum chronicus, rheumarthritis chronica) is a subacute inflammation of one or more joints. It sometimes occurs as a residue from an attack of acute rheumatic polyarthritis, or some other form of acute articular inflammation (*e. g.*, gonorrhœal arthritis), or it may, in a small proportion of instances, originate independently from causes of a "rheumatic" order.

In marked contrast to acute rheumarthritis, the present disorder is almost exclusively confined to the latter half of life. It is especially prone to occur in those who have gone through repeated attacks of rheumarthritis without the supervention of cardiac or other complications tending to a fatal issue. It is most commonly localized in those joints, viz., the knee, ankle, and the larger articulations of the upper limb, which are usually attacked in rheumarthritis. Whatever hinders the complete restoration of the joints during the acute disease—violence of local inflammation, unsuitable regimen, constitutional weakness, etc.—will therefore act as a cause of the chronic malady. But even when recovery is complete, acute polyarthritis leaves a tendency to subsequent disease in the affected joints; like any other organ which has once suffered, they become a *locus minoris resistentiæ*, peculiarly sensitive to external influences of an injurious kind. Among such influences, the following are pre-eminent: prolonged exposure (for weeks or months) to cold and damp air in bedroom or workshop, laboring in the water or in wet places, etc. These influences are usually looked upon as the causes of the malady even when this arises independently of previous rheumarthritis; and not without reason, for chronic rheumatic arthritis is mainly a disease of the poor—of those who are habitually exposed to such agencies. It is usually the joints which are immediately exposed to cold and damp that become affected: in maid-servants, who stand barefoot on damp floors, the ankles; in washerwomen, the wrists; in persons who expose one side of the body more than the other to damp and draughts (*e. g.*, persons whose bed stands against a damp wall), the joint-affection is usually one-sided, etc.

These facts all tend to show that chronic rheumatic arthritis is a purely local disease, having nothing in common with acute rheumarthritis beyond its articular localization, and standing in much the same relation to it as that in which a chronic bronchitis or conjunctivitis stands towards measles; with this difference, however, that bronchial and conjunctival catarrh are far more frequently independent of an attack of measles than chronic articular rheumatism of previous rheumarthritis. Otherwise, the relation in the two cases is the same. Just as the pathological changes connected with measles become localized in the mucous lining of the respiratory organs, and leave increased liability to disease behind them, so rheumarthritis gives rise to mischief in the joints and leaves behind it a tendency to subsequent attacks of an independent order. Moreover, the entire course of chronic rheumatic arthritis, as we shall presently see, stamps it as a purely local disorder, confined to one or several joints.

Morbid Anatomy.

The structural changes are those of chronic inflammatory irritation, attended by proliferation and thickening of the cartilaginous and synovial tissues, extending subsequently to the capsule of the joint and the neighboring structures, but showing little tendency to the formation of a liquid exudation, especially of a purulent kind. Owing to the development of dense cicatricial tissue, the membranous elements of the articulation become thickened and rigid; they may coalesce with the soft parts lying over them; the villous processes in the interior of the joint become tough and hypertrophied; the cartilages are frayed out, undergo fatty change, and are more or less worn away. The amount of fluid in the joint is often very trifling, and consists of a thickish gruelly matter containing tissue-*débris* and oil-globules; should the inflammatory changes have undergone exacerbation, it may be more abundant and of a serous character. In old and very obstinate cases, the disturbances of nutrition may extend to the bones and the soft tissues surrounding the joints; the whole region is greatly thickened; abnormal adhesions may form and more or less complete ankylosis may result. In some few cases the morbid changes that are characteristic of arthritis deformans may be developed, such cases forming a connecting link between the two diseases.

Symptoms and Course.

The symptoms are all derived from the condition of the joints and the troubles to which this gives rise. One or more joints are almost continually tender; from time to time they become the seat of more acute pain, which comes on either spontaneously or in consequence of pressure and movement, and which usually radiates beyond the joint into the soft parts of the extremities. The pains are generally most acute during cold and wet weather; indeed, cold in any form seems to aggravate them, while heat, especially dry heat, gives relief. The joint is more or less swollen, in proportion to the severity of the local mischief; sometimes, when the inflammation has been aggravated by muscular exertion or injury, the joint feels hotter to the hand, and may, if superficially placed, exhibit slight fluctuation. At other times we perceive an abnormal degree of resistance to passive movement, and more or less distinct crepitation, giving the impression of adhesions being torn through or of rough surfaces grating on each other; this is often felt by the patient himself when he tries to move the affected limb. The stiffness and grating are always most marked after the joint has been allowed to remain at rest for a time; hence, many patients find their troubles increased by a night's repose. It is not till after the joint has been in use for some little time that it regains its suppleness and the grating is diminished,—as though some obstacle had been got rid of. Many patients find their affected joint a sort of barometer; they are warned of an approaching change in the weather, a day or even longer beforehand, by pain or other abnormal sensations. This is by no means a delusion on the part of the patient, as is often supposed; I have myself seen undoubted examples of such prophetic joints. As the joint is unquestionably influenced by the pressure of the atmosphere, we may readily conceive that changes in the pressure, by causing variations of tension in the irritated and sensitive nerve-fibres of the affected joint, may be perceived by the patient more easily than by a healthy person.

Fever is either quite absent, or occurs now and then in a mild form, when the inflammatory changes undergo exacerbation, or when several joints are affected at once. None of the other functions are in any way disturbed.

The inflammation never shifts suddenly from one joint to another, as in acute polyarthritis; on the contrary, it may remain limited to one particular joint for months and years, when the patient has been withdrawn from the causes of the malady; but when these causes continue in operation, fresh joints are successively attacked, without any simultaneous remission of symptoms in those previously diseased. Again, chronic rheumatic arthritis is never complicated by inflammation of internal organs. It is not unusual, indeed, for an attack of acute rheumarthritis to occur in a patient already suffering from the chronic disease, especially if he has been similarly attacked before; in such cases, of course, the acute disorder brings its own complications with it. In these intercurrent forms of rheumarthritis the first joints to be attacked are usually those which are already affected by chronic inflammation; and thus many physicians are led to believe, quite wrongly, that chronic rheumatic arthritis, like the acute disease, is of constitutional origin, and attended by a liability to cardiac complications.

The sole complication which may perhaps be allowed to stand in connection with the disease now under consideration is a painful state of the muscles ("muscular rheumatism"), which is partly due to the same causes, and may therefore precede, accompany, or succeed the articular affection. But the muscular pains in the neighborhood of the inflamed joints are certainly due, in many cases, either to an extension of the inflammatory mischief to the tendons and intermuscular connective tissue, or to stretching of nerve-fibres running in the thickened tissues of the joint. Such pains cannot be regarded, strictly speaking, as a complication.

The disease runs a very tedious course, with alternate periods of remission and exacerbation, connected, as I have already shown, with atmospheric changes and with the hygienic surroundings of the patient. In rare instances, and only when a particular joint is left unrestored to its normal condition after acute polyarthritis, do we find the disease subsiding entirely after some weeks; but this speedy recovery is only possible under a combination of favorable circumstances, and it is rarely permanent. As a general rule, the disease drags on for months and years, terminating—even in the most satisfactory cases—in imperfect recovery; imperfect, either because limited to some only of the affected joints, or because the process of repair is arrested at a certain point in all, and a considerable degree of thickening remains. In a few exceptionally severe cases the joints become ankylosed, the muscles atrophied, and the entire limb wastes away, making the swollen joint appear still more prominent. Nay, there have been solitary instances in which the unhappy patient, owing to multiple ankylosis of the joints of both upper and lower extremities, has become quite helpless and incapable of movement.

Diagnosis.

It is usually an easy matter to recognize chronic rheumatic arthritis, more particularly in the numerous cases in which it is left as a residue of acute rheumarthritis. When there is any difficulty, we depend for a correct diagnosis chiefly on the exclusion of all other causes but those of an atmospheric kind, capable of setting up chronic inflammation in one or more joints. If we take into account the patient's history, age, and occupation, the effect of the weather on his symptoms, the fluctuating course of the malady, the absence of suppuration, etc., we can hardly fall into the error of confounding chronic rheumatic arthritis with traumatic, scrofulous, or other affections of the joints. It may be distinguished from arthritis deformans by the way in which it often grows out of an attack of acute rheumarthritis, by its being usually limited to one, or, at most, to a very few joints, by its unsymmetrical character, and by its not causing the deformities characteristic of the latter disease; but before the deformities have had time to be developed it is impossible to distinguish with certainty between the two affections, and they are often confounded with each other. It may be, too, that chronic rheumatic arthritis is capable of passing into arthritis deformans, the slow inflammatory process leading on, under particular conditions, to those structural alterations which occasion the characteristic deformities of the latter malady.

In distinguishing chronic rheumatic arthritis from the articular neuroses, we have to bear in mind (apart from the points already referred to) that, in the latter group of disorders, the subjective symptoms (such as pain, etc.) are strikingly disproportionate to the objective phenomena presented by the affected joint. Moreover, the cutaneous sensibility is in an abnormal state (hyperæsthesia, anæsthesia, etc.).

Prognosis.

This is very favorable as regards danger to life, very unfavorable as regards the prospect of complete recovery. It is only in comparatively recent cases, when the patient is able to withdraw himself from all hurtful conditions, that a more or less satisfactory and lasting degree of improvement can be attained. In the majority of cases we must be content with procuring temporary alleviation.

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Treatment.

The prophylaxis of chronic rheumatic arthritis flows naturally from what has been said above concerning its causes. It is in most respects the same as that of rheumarthritis. Patients who have already suffered from the latter disease should be advised, in order to ward off chronic articular rheumatism altogether, or its exacerbations when it is already established, to live in a dry, warm house, and to seek change of climate, either for a time or permanently, when that under which they live is unfavorable.

The actual treatment of the disease embraces internal remedies and external applications. The former used at one time to be largely employed, in the belief that the disease was of constitutional origin, due to a "rheumatic diathesis," and therefore amenable to "antirheumatic" treatment. I have been at some pains to show that chronic rheumatic arthritis is, on the contrary, a purely local disorder, and that we cannot assume anything more than the existence of a tendency on the part of some particular joint to become inflamed. Hence, the administration of internal remedies, so far, at any rate, as they are meant to combat a rheumatic diathesis, is wholly objectless. Indeed, we may safely conclude that all the drugs reputed to be useful in this complaint continue to be given, not from any faith in their power to do good, but from habit, and because no better substitutes are known to us. Most of them have, in fact, been abandoned—*e. g.*, guaiacum, corrosive sublimate, and arsenic; only colchicum and aconite have kept their place—perhaps in virtue of their narcotic properties, even these being usually prescribed, to make assurance doubly sure, in combination with tincture of opium, when they may certainly be allowed to exert an anodyne effect.

Remedies calculated to improve nutrition are of far greater consequence, for most of the sufferers belong to the poorer class and are in broken health. Such remedies may indirectly promote the subsidence of local inflammation. Cod-liver oil and the preparations of iron and quinine stand foremost in this respect; their operation should be assisted by suitable diet. When the patient's general health is good, we may venture to give iodide of potassium for long periods of time, in order to promote absorption.

Local applications alone are far more efficacious than any internal remedies; they should never be omitted. Their object is, on the one hand, to remove the inflammation and swelling of the joints, on the other, to alleviate pain or other annoyance.

In recent cases, or when exacerbations occur, the inflammatory symptoms must be treated on the principles already laid down for the management of delayed recovery of single joints after acute polyarthritis (p. 71); but the process being more sluggish, cold applications are less suitable, and are often badly borne; local blood-letting, too, should be avoided. On the other hand, counter-irritation is often useful; it should be employed, especially in inveterate cases, were it only because the dilatation of the cutaneous vessels creates a feeling of warmth which is agreeable to the patient. Painting the joint with iodine, rubbing it with alcoholic, ammoniacal and camphorated liniments (soap liniment, volatile liniment, opodeldoc, etc.), with turpentine, petroleum, spirit of mustard, etc., are often prescribed; the patient frequently employs these measures on his own responsibility, on account of the temporary relief afforded by them. Wrapping up the joints in materials which keep them warm and exert a mild stimulating effect upon the skin, is likewise grateful to the patient. I allude to many of the plasters in repute, to tow, cotton-wool, fur, etc. When the pain is more acute, these measures may be supplemented by the use of stimulant and narcotic liniments (*e.g.*, that recommended by Niemeyer: Veratrine, from six to nine grains; chloroform, half an ounce; Hoffman's balsam of life,[1] fifteen drachms; or one of the liniments described above, with the addition of tincture of opium in the proportion of one to five). A hypodermic injection of morphia in the immediate neighborhood of the painful joint is always, however, more effectual. Hypodermic injections of carbolic acid (p. 68), or injections into the articular cavity itself, as advised by Hueter, may be tried.

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[1] A preparation of the German Pharmacopœia, consisting of an alcoholic solution of Peru balsam and seven aromatic oils.

Warm baths, both local and especially general, enjoy the highest reputation among remedies for this disease. Their value in relieving pain and causing the structural changes to subside, does not depend, either wholly or chiefly, on their chemical composition. Prolonged immersion in plain water at a temperature of from 28° to 30° Réaumur (95° to 99° F.), or even higher, is often most beneficial. We may safely ascribe the good effect, at least in part, to the influence exerted by the baths on the nutritive processes, especially by exciting secretion, and to their topical action in dilating the blood-vessels, and thus modifying the circulation through the affected part, and saturating the tissues with moisture. These effects may be supplemented by many others (*e. g.*, the production of electrical currents, according to Scoutetten, Heymann, and Krebs), which, though individually trifling, may aid one another by their simultaneous and concerted operation. Whatever constituents the baths may contain besides hot water may broadly be said to act by stimulating the sensory nerve-ends in the skin, either momentarily, or—when the body is immersed for a long time in water containing salts which impregnate the skin—during a longer period of time. This stimulation exerts an influence on the functions of circulation and respiration, and also, perhaps, on that of secretion. The precise nature of the irritant—whether it consist of salts or gases in solution (*e. g.*, carbonic acid, sulphuretted hydrogen), or of mustard, fir-needles, aromatic and balsamic matters—is of little moment. Peat- or mud-baths are among the best, because they contain the largest proportion of salts, gases, and other irritating ingredients, whose influence in causing absorption may be increased by friction of the affected joints; they are, however, often ill borne by weakly and excitable subjects. For the rest, in choosing such additions to artificial baths, and in our choice of natural thermal springs, we are guided rather by accidental and collateral considerations, than by any belief in the specific virtue of one or other of their constituents.

Those natural springs whose reputation is of long standing, and which really possess a healing power, are all remarkable for their high temperature; this is the only feature they have in common; they differ widely in their chemical composition, belonging either to the group of indifferent thermal waters, or of sulphuretted, saline, or alkaline waters. The favorite baths in Germany and Switzerland are: Pfaeffers and Ragatz, Gastein, Wildbad, Roemerbad, Leuk, Teplitz, Warmbrunn, Baden (near Vienna), Baden (in the valley of the Aar), Baden-Baden, Landeck, Schinznach, Aix-la-Chapelle, Wiesbaden, and other hot brine springs (Nauheim, Oeynhausen); in France: Plombières, Aix-les-Bains, Barèges, Bagnères de Luchon, Néris, Luxeuil, Mont-Dore, etc.; in Hungary: the highly curative Hercules baths in Mehadia, Trentschin, etc. No stringent rules can be laid down for the choice of one or other of the baths in this long catalogue; in a general way, those springs which are most rich in solid matter (especially concentrated brine-springs) are most suited to those cases in which we wish to stimulate absorption; while those containing less saline matter—the more indifferent waters—are more useful for soothing and alleviating pain. Of course, the operation of the natural waters is well known to be aided by a variety of collateral circumstances, such as climate, etc., involved in residence at a bath, and which often exercise a more favorable influence on the general state of the patient's nutrition than the mere use of the same waters, or of artificial baths of identical composition, at the patient's own home.

It is obvious that treatment by local baths must be restricted to a few only of the joints. They may serve to assist the action of general baths in promoting absorption; or they may be employed when, for any reason, the use of general baths is inadmissible; when, for example, there exists some valvular lesion of the heart, possibly bequeathed by a previous attack of polyarthritis; or when the vessels are diseased; or, in short, when there is any condition that forbids the employment of general baths of a high temperature and highly charged with gas. The operation of local, like that of general baths, may be assisted by adding various stimulant ingredients, especially peat or mud, to the water; and their temperature, owing to the limited extent of surface exposed to them, may be higher than that of baths in which the whole body is immersed, thereby increasing the activity of local perspiration and absorption. Hot sand-baths are very efficacious—I have myself seen admirable results from their systematic use; and they are especially fitted for patients in humble circumstances, on account of the ease with which they may be procured.

To cause perspiration, and thereby to promote the absorption of exuded matters, is likewise the essential object of vapor-baths and of the methods employed in hydropathy, viz., the wet pack, rubbing and douching with water; but such methods should be employed with caution, and reserved for recent cases of the disease in strong and otherwise healthy subjects; or we may employ them tentatively, when other curative measures have been tried and have failed. So, too, the natural vapor-baths of Monsummano, which have lately come into fashion, should be resorted to with the utmost caution. They certainly cause very profuse perspiration, but at the same time they excite the circulation in an alarming degree.

Good effects have recently been obtained from electricity, in the form of the continued current passed through the affected joints. Pain has been relieved, and the swelling and inflammation have abated. Fumigation of the joints with resinous and balsamic vapors (benzoin, camphor, frankincense, amber, etc.) is still largely resorted to, especially by the laity, for soothing pain. The "animal baths" (Thierbaeder) which were at one time so popular, have now passed into the category of historical curiosities.

In very severe and inveterate cases, when ankylosis and malposition of the joints have already taken place, orthopædic methods may still accomplish favorable results, such as a restoration of the limbs to usefulness. (See Volkmann, loc cit., p. 520.)

III. Myopathia, seu Myalgia Rheumatica.

(Muscular Rheumatism.)

Literature.—In addition to the works enumerated under Acute Rheumatic Polyarthritis and in the introductory section, we have the following: *Froriep*, Die rheumatische Schwiele. Weimar. 1843.—*Valleix*, Etudes sur le rhumatisme musculaire. Bull. gén. de Thérapeut. 1848. Octobre, Novembre.—*Virchow*, Archiv für pathol. Anat. IV. 262.—*Oppolzer*, Allgemein. Wiener med. Ztung. 1861. Nos. 36 and 37.—*Beau*, Archives géner. de Médecine, December, 1862.—*M. Rosenthal*, Œsterreich. Ztschrift. für pract. Heilk. Decr. 1864.—*Runge*, Natur und Behandlung des Hexenschusses (Lumbago), Deutsche Klinik, 1867, No. 3.—Also text-books on surgery, and works on diseases of the nervous system and on electro-therapeutics.

In the existing state of our pathological knowledge, it is impossible, as I have already remarked, to construct an adequate and scientific definition of all the maladies included in the group of rheumatic myopathies—taking the word in its narrower sense, as synonymous with the old term, "muscular rheumatism." It is impossible, because all the painful affections of the muscles, their tendons and fasciæ, of whose etiology or morbid anatomy, or both, we are ignorant, and which we are therefore unable to classify under any of the recognized pathological categories, are thrown into this group. Our only excuse for maintaining such a group at all lies in our ignorance of certain diseases associated with muscular pain, and in the practical necessity of giving them a name of some sort. No sooner is the morbid anatomy of one of these affections understood, or a tangible cause for it discovered, or its symptomatic relation to some other disease ascertained, than it is at once excluded from the domain of "muscular rheumatism." I need only refer, by way of illustration, to the "metallic," "scorbutic," and other forms of rheumatism recognized by the older schools of medicine; as soon as their connection with metallic poisoning, scurvy, etc., had been made out, they were summarily withdrawn from the "rheumatic" class. So, too, there can be no doubt that trichinosis must over and over again have been called "muscular rheumatism" before its true nature was understood; nay, even those muscular affections that are unquestionably due to "rheumatic" influences are separated from "rheumatism" as soon as their morbid anatomy has been made out. Thus, any muscular disorder proved by its course and issues to be really inflammatory is called "myositis," not "muscular rheumatism." We speak of a "purulent," "fibrous," "ossifying" myositis. Even when inflammation of single muscles, such, *e. g.*, as those of the tongue or the psoas, is due to chill or to some unknown cause, we term the malady "glossitis," "psoitis," because we are aware of their inflammatory character, and, on the strength of this knowledge, separate them from the group of obscure affections included under "muscular rheumatism."

It is supposed that the structural changes in the affected muscle are wrought by processes of an inflammatory kind, situated either in the muscle itself, or in its sheaths and fasciæ. This view rests on the observed fact that circumscribed thickenings of the interstitial connective tissue, Froriep's "fibroid patches" (rheumatische Schwielen) have occasionally been met with in muscles long subject to "muscular rheumatism." In most cases, however, nothing of the sort can be discovered after death; and since, even during life, the disorder is not attended by any sign of inflammation except pain, or at most by some thickening of the muscle—a thickening which may be due to contraction—we are constrained to believe that the pathological changes consist either in a mere transient disturbance of the circulation, such as hyperæmia, or in slight serous exudation, which is readily absorbed, or, lastly, in some affection of the intramuscular terminations of the sensory nerves which is purely neuralgic. That many forms of "muscular rheumatism" are indeed rather of nervous origin than dependent on inflammatory changes in the muscular or the interstitial connective tissue, is proved by cases in which superficial muscles, readily accessible to examination (*e. g.*, the sterno-mastoid) are attacked by rheumatism. We find the muscle spasmodically contracted, but not, as a rule, more painful than any uninflamed muscle in a state of tonic spasm; moreover, the muscle is not nearly so tender to the touch as it would be if really inflamed, pain being caused only by attempts at forcible extension; hence, we conclude that the case is one of simple tonic spasm. Only the influence of tradition, handed down from a time when the domain of "rheumatism" was even wider than it now is, prevents us from including this "Torticollis rheumaticus" among the varieties of idiopathic spasm, instead of retaining it among those of "muscular rheumatism." The darkness which overhangs the whole subject is rendered yet more dense by such anomalies as this.

Etiology.

Here, too, there is endless confusion, kept up by the fact that the "rheumatic" causation of the muscular affections belonging to this group is not rigorously defined. Diseases that are, strictly speaking, not of rheumatic but of traumatic origin, find themselves included under the head of "muscular rheumatism." I need only mention many cases of so-called "lumbago" (*Myalgia lumbalis*). The sole reason that can be adduced in support of this practice is that the injury which precedes the symptoms is not, as in other traumatic maladies, extraneous, but arises from the movements of the body itself; it thus escapes observation—rough observation, that is—and the malady is attributed to some of those unknown noxæ which are grouped together with chill, under the "rheumatic" category. It may be, too, that these disorders are included among the obscure myopathies because the trifling nature of the structural lesion by which they are occasioned renders it rather probable than proved to exist.

Symptoms.

Pain is the one really characteristic symptom. It comes on of its own accord, and may be excited by movement and pressure. If we put aside the forms of the disease alluded to above, which rather belong to the group of "rheumatic spasm," pain is common to all the disorders included under "muscular rheumatism." Apart from pain there is nothing characteristic about these myopathies, save perhaps their dependence on the weather;

and this is not always obvious. They may last for days or weeks; usually unattended by fever, they may cause slight pyrexia in very susceptible individuals, or when many muscles are simultaneously involved. They are not followed by any sequelæ; indeed, the occurrence of sequelæ overthrows the original diagnosis of "muscular rheumatism." Muscles which have once been affected are peculiarly liable to become affected again; in such cases "fibroid patches" may occasionally be developed. Further details may be reserved for the ensuing description of special forms of myalgia.

Diagnosis.

What I have said above is enough to show the importance of excluding all other affections that may give rise to muscular pain. Such pain is a very common symptom of many local and constitutional disorders at some period of their course, and especially before their characteristic signs are manifested; this accounts for the ease with which both lay and professional opinion may be misled into ascribing muscular pain and cramp to "muscular rheumatism," when they really form part of some wholly different malady. Such "rheumatoid" pains—sensations of dragging and tearing in the muscles—are most frequently associated with disease of the vertebral column and spinal cord, and with certain forms of chronic poisoning by lead and mercury. We should always be on the lookout for such causes, especially when the lower extremities are symmetrically involved; for idiopathic affections seldom occur in the lower limbs, and when they do are usually one-sided. Of acute disorders the exanthemata (especially small-pox) and trichinosis—the former at their outset, the latter during its course—are prone to be attended by pain in the muscles, more or less generalized. Again, painful spasm of the muscles is often of reflex origin, caused by deep-seated inflammation or painful affections in their neighborhood; some such mischief ought always to be suspected when spasm is associated with muscular pain. Finally, muscular rheumatism may be confounded with neuralgia, particularly when the symptoms of the latter are indefinite, when deep-seated nerves are involved, when the pain fails to correspond to the course of a particular nerve-trunk, and radiates over a wider area.

Treatment.

As a general rule, the patient ought to be kept warm and induced to perspire freely (in recent cases) by the administration of hot drinks, with or without the addition of diaphoretic remedies (liquor ammoniæ acetatis, Dover's powder, etc.) or by means of vapor-baths or wet-packing. Other measures, whether antiphlogistic, derivative, or merely sedative, are indicated by the seat and duration of the malady.

In order to prevent, as far as possible, any return of the pain in muscles which have previously suffered, we must pay special attention to the various "roborant" methods by which the body may be inured to cold and other outward hardships. Rubbing with wet towels, the cold douche, cold baths, especially sea-bathing, may be recommended for this purpose; the patient should be advised not to coddle himself up in furs and thick garments, nor to be afraid of fresh air, but to accustom himself, prudently and gradually, to do without excessive precautions against cold.

I will now proceed to describe the more usual forms of muscular rheumatism.

1.—Myalgia Cephalica s. Capitis.

(Rheumatic Cephalalgia. Rheumatismus Epicranii. Rheumatism of the Head.)

Localized in the muscles of the occipital, frontal and temporal regions, and in the pericranium. Movements of the head, pressure of comb or head-gear, cause sensible and sometimes very severe pain. This affection may easily be mistaken for periostitis, hemicrania, or headache due to intracranial mischief; perhaps it may be more correct to say that these disorders are frequently mistaken for "rheumatism" of the head. It is not until they have all been excluded, and the pain shown to be symmetrical and really localized in the muscles or the fibrous aponeurosis by the effect of movement in exaggerating it, that we are sure of our diagnosis of myalgia.

For the treatment of this disorder, when recent, leeches behind the ears, or on the forehead and temples, are recommended, to be followed up by diaphoretic measures. When the malady is obstinate we have recourse to blisters or the continued current, together with opiates internally, or hypodermic injections of morphia to allay pain. The injection of carbolic acid, under the skin or into the tissues, may possibly turn out to be as useful in this as in the other forms of which I am about to treat.

2.—Myalgia Cervicalis, Torticollis Rheumaticus.

(Rheumatism of the Cervical Muscles. Cervicodynia.)

This name is given to the painful idiopathic rigidity of one or more muscles of the neck or nape, in consequence of which the head is either fixed immovably between the shoulders, or—when the disorder is one-sided—obliquely twisted, with the occiput towards the affected, the face towards the sound side (Torticollis, Caput obstipum). The affected muscles may usually be seen or felt like cords under the skin. Pressure along the edges of the spinal column, perhaps over the points where the nerves enter the muscles, is usually more painful than pressure upon the muscles themselves. The disease is easily recognized by the peculiar attitude of the patient, and the way he turns his whole body at once instead of rotating his head. It is tolerably common in children, the other muscles of the trunk and limbs being principally affected in adults. It is of importance to ascertain, when the spasmodic contraction first shows itself, whether it be really an idiopathic disorder of the muscles or nerves (spinal accessory and upper cervical nerves), or a result of reflex irritation from disease of the vertebræ, or else a contraction secondary to paralysis of the antagonist muscles. The sudden onset of the symptoms, usually preceded by exposure to a draught or by some unaccustomed craning of the neck, together with their rapid course and favorable issue, furnish materials for a diagnosis in doubtful cases.

When the disorder is one-sided, it may generally be cured by keeping the neck warm with flannel, etc., or by means of hot poultices or the wet pack. The symptoms may be relieved and often quickly removed by rubbing the rigid muscle with the hand, either with or without the aid of opiate embrocations. Careful and gradual extension of the muscle by passive traction of the head towards the healthy side is sometimes of service. If the cervical muscles are symmetrically and largely involved, the disorder may be cured by cupping, wet or dry (according to the local sensibility and constitutional state of the patient), or by other measures of a derivative kind, such as mustard plasters, stimulating liniments, etc. A speedy cure is often wrought by brushing the skin, till it is thoroughly reddened, with the electric brush. In other cases, the continued current yields excellent results. Finally, a subcutaneous injection of morphia may prove to be indispensable in this as in the previous disorder.

3. Myalgia Pectoralis et Intercostalis.

(Pleurodynia, Rheumatism of the Pectoral and Intercostal Muscles.)

The affected muscles are painful, the pain being usually diffused over the whole of one side of the chest, and aggravated by the respiratory movements, by coughing, sneezing, and defecation; when the pectoral muscles are specially involved, by movements of the upper arm likewise. From pleurisy this affection may be distinguished by the absence of fever and cough, and the physical signs of intrathoracic mischief; from intercostal neuralgia, by the absence of "tender points" (*points douloureux*), and by the diffuse character of the pain, which, in the latter affection, radiates from the spine towards the sides and front of the chest along the course of the nerves; from periostitis of the ribs, by the fact that in this disease the pain is more intense, aggravated by pressure on a part of the rib itself rather than on the intercostal spaces; by its being attended with fever and often with œdema of the overlying skin; finally, by the difference in the previous history of the case.

The pain may be quickly relieved, as a rule, by dry or wet cupping, with warm applications to the surface, or by a subcutaneous injection of morphia. Should these means fail, we may resort to counter-irritation by mustard poultices or blisters, or by the induced current. The same treatment is found effectual in the next disorder on our list.

4. Myalgia Scapularis (Omalgia, Scapulodynia).

Here the muscles attached to the humerus and scapula are painful and rigid.

5. Myalgia Lumbalis.

(Lumbago, Rheumatism of the Lumbar Muscles.)

This is characterized by pain, more or less acute, setting in of a sudden in the soft parts—the muscles and fasciæ—on one or both sides of the lumbar spine. When at all severe, this malady is the most serious to the patient of all those included in the present group, since hardly any posture gives relief and every movement causes pain. Of all the varieties of myalgia, this is the one which may most often be traced to a traumatic cause, viz., to strain and possibly rupture of single muscular fibres occurring when the patient has been stooping down or regaining the erect posture, raising weights, riding, etc. In other cases, however, the malady is unquestionably brought on by cold and damp; *e. g.*, it is not unusual for persons who have fallen asleep on damp ground to find, when they awake, that they are unable to get up, owing to lumbago.

Many diseases, setting in with pain in the loins, may be confounded with this variety of idiopathic or rheumatic myalgia. Such mistakes are all the more likely to occur, as the lumbago is not unfrequently attended by slight febrile disturbance, making the patient restless and robbing him of his sleep. Many acute infective disorders, as *e. g.*, small-pox, are ushered in by similar pains, which are often attributed to "rheumatism" before the eruption makes its appearance. Diseases of the kidneys, the uterus, the vertebral column, the spinal cord and its membranes—especially the spinal congestion so common in sufferers from hæmorrhoids—may all give rise to similar errors of diagnosis. The simple enumeration of all these disorders is a sufficient warning to the physician that he must be cautious in ascribing pain in the loins to lumbago. Besides the absence of symptoms pointing to any one of these disorders, special stress may be laid on the suddenness with which the pain comes on, the tenderness on pressure of the muscles, and finally the existence of one of the usual causes of myalgia.

Lumbago is more common in the male than in the female sex, doubtless because men are more exposed to its exciting causes. It is more prone to become chronic and to recur than any other form of "muscular rheumatism." For this reason, and also on account of the annoyance and suffering it inflicts, it should be vigorously treated from the outset by those measures which I have recommended for the more severe variety of cervical myalgia.

Besides the muscular groups alluded to above, any muscle in the body is liable to be affected by "rheumatism." Some authors, especially the older ones, go so far as to speak of "rheumatism of organic muscles" (uterus, diaphragm, heart, intestines, bladder, etc.). These affections are all characterized by a single feature, viz., pain, which is referred, with more or less show of justice, to the muscular tissue. There is no way of distinguishing them, when they occur in the organic muscles, from neuroses (colic, cardialgia, angina pectoris), or even from true inflammation; this is the less important as the treatment is the same for all.

Again, under the name of "vague muscular rheumatism," we are acquainted with wandering pains, now in one muscle, now in another, or in the tendons and fasciæ; these pains may occur either with or without fever; they are termed "vague muscular rheumatism" when no cause for them can be assigned, or when they are preceded by a chill. They often put on a neuralgic character and may alternate with true neuralgia (*e. g.*, of the fifth nerve). Sometimes, after shifting from place to place, the pain settles in some particular group of muscles, or is limited to the area of distribution of a particular nerve.

When no cause for the pains can be made out, and there is no special indication for treatment, diaphoretic measures (when the case is recent) are usually found sufficient, in combination with friction of the painful parts with gently stimulating, aromatic waters and liniments, such as are used in chronic inflammation of the joints. Should the pain become acute, narcotics may be applied locally or given internally. In chronic cases of this and all other forms of myalgia, the remedial measures to be adopted are the same as those enumerated above under chronic rheumatic arthritis.

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Of those muscular affections whose morbid anatomy has been more fully explored, and which are, therefore, excluded from the domain of "muscular rheumatism," only a small proportion come within the province of the physician, unless when they happen to form part of some constitutional malady, acute or chronic, or depend on disturbances of innervation. To this symptomatic group belong hemorrhages into the muscular tissue, occurring in connection with scurvy, hæmophilia, and purpura, and in the severer forms of acute infective disease (typhus, enteric fever, variola, etc.) and in some kinds of poisoning (*e. g.*, by phosphorus); also the suppurative inflammation leading to abscess, met with in pyæmia, septicæmia, and glanders; also the degenerative changes of the muscular tissue in various severe forms of infection and poisoning. Progressive muscular atrophy and pseudo-hypertrophy are connected with disorders of innervation, as also the more partial forms of atrophy limited to single muscles or groups of muscles. These affections are all described elsewhere. Those muscular disorders of a more independent kind that still remain, are either of purely surgical or pathological interest (*e. g.*, congenital abnormalities, fibrous and ossifying myositis), with two exceptions: inflammation of the tongue (glossitis), which finds its place among the diseases of the digestive apparatus, and inflammation of the psoas (psoitis), which I now proceed to describe.

Psoitis and Peripsoitis.

LITERATURE.—*Fordyce*, Elements of the Practice of Physic, London, 1784.—*Sauvages*, Lumbago psoadica in Nosolog. method. Clas. VII., Gen. XXX.—*C. G. Willert*, de Psoitide. Diss. inaug. Berlin, 1830.—*S. G. Vogel*, Handb. d. prakt. Arzneiwissensch. Wien, 1832. IV. p. 248.—See also *Pitha*, Handb. d. allgem. u. spec. Chirurgie, IV. 1. p. 206, and *Volkmann*, loc. cit., p. 850.

The inflammation has its seat in the interstitial connective tissue of the muscle, the *perimysium internum*, and in the muscular fibres proper—the primitive bundles; but it remains a question whether the latter with their sarcolemma are primarily affected, or only secondarily involved in the inflammation of the connective tissue. Apart from those cases of circumscribed abscesses in muscle caused by embolism and metastasis, apart from the gravitative abscesses which often travel along and through the psoas, we have cases in which inflammation is propagated to the muscle from the neighboring bones or soft parts, *e. g.*, from carious lumbar vertebræ or ilium, or from inflammatory mischief in the pelvic viscera or the areolar tissue around them. Psoitis also occurs, though more rarely, as an independent disease, when it may usually be traced to violent exertion, straining (during parturition or gymnastic exercises), or even to direct contusion. Finally, it may occur without any discoverable cause, and is then commonly viewed as "rheumatic" or due to chill.

The inflammation almost always ends in suppuration. Under favorable conditions this may remain circumscribed, and finally lead to cicatrization with more or less permanent loss of substance; or the pus may become inspissated and enclosed in a capsule. More commonly, however, the suppurative process is diffuse and extends to the neighboring connective tissue after having destroyed the muscle; it then eats into the bones, or burrows forward under Poupart's ligament or through the retroperitoneal areolar tissue into the soft parts of the back; or it may perforate the bladder or intestine, or the vagina in women; in a few very exceptional instances it makes its way upward and penetrates into the cavity of the pleura.

Symptoms and Course.

The most prominent symptoms are pain on movement of the corresponding thigh, and the peculiar position assumed by the latter; since active contraction of the inflamed muscle is as painful as its passive extension, the patient instinctively tries to relax it as much as possible, by keeping the thigh (when in the recumbent posture) flexed at the hip-joint and rotated outwards; or, if compelled to walk, by keeping the trunk bent forward and advancing the thigh at each step by twisting the pelvis on the lumbar part of the vertebral column, or even by lifting the thigh with the hands. The peculiar position of the limb is not unfrequently associated with spasmodic rigidity of the affected muscles, due to reflex irritation of sensory nerve-ends, or to direct irritation of the motor fibres or of the muscular tissue itself. When the abnormal position of the limb is maintained for any length of time, shortening of the muscle may take place even without cicatricial shrinking; just as a healthy muscle, kept permanently shortened, will accommodate itself to the approximation of its points of attachment, and gradually diminish in length in consequence of structural changes of an unknown kind in its tissue.

Apart from the pain in the muscle itself which is brought on by any attempt to move the thigh, we often find very characteristic pains of another kind occurring spontaneously in the course of the nerves which perforate the psoas, viz., the ileo-hypogastric, ileo-inguinal, genito-crural, and external cutaneous; these pains are localized in the lower part of the abdominal integument near the *mons veneris*, in the skin of the scrotum and about the root of the penis in males; in the *labia majora* in females, or in the skin clothing the outer surface of the thigh.

Under favorable circumstances, *i. e.*, when the abdomen is not too tympanitic or the bowels too full, we may succeed, after suppuration has occurred, in detecting the abscess in the muscle by palpation.

Fever is almost always present from the outset. It is of no regular type, save when pus has already formed in the muscle; the temperature then exhibits the usual fluctuations of suppurative or pyæmic fever. When the psoas is secondarily invaded by some abscess already existing in its neighborhood, it is clear that suppurative fever may show itself before the suppurative process in the muscle itself begins.

It is only in those comparatively rare cases in which the psoitis occurs as an idiopathic disorder due to rheumatism or to injury, that the disease takes a favorable course and terminates in complete recovery. Should the inflammatory process not have run on to suppuration, recovery may take place in about a week's time; more frequently, however, pus forms, and several weeks are taken up by convalescence. When the disease of the muscle, as is most usual, is secondary to some other mischief in its neighborhood, its course and issue will depend upon the nature of the primary affection. As a general rule in these cases, the patient succumbs to exhaustion brought on by the continual drain of pus.

Treatment.

In recent cases of traumatic or rheumatic origin, the inflammation should be combated by local bleeding (leeches to the groin, cupping over the lumbar region on the affected side), inunction of mercurial ointment, and cold or hydropathic compresses. The affected limb must be kept absolutely quiet, a measure which the patient adopts instinctively for the relief of his sufferings. As a rule, it is impossible to avert suppuration; hence, warm fomentations may be resorted to at an early stage, and are more agreeable to the patient than cold applications, because they help to allay the pain. As soon as an abscess can be distinctly made out, it should be opened. Its further management must conform to ordinary surgical principles.

When the inflammation has been propagated from the adjacent pelvic viscera (intestine, uterus, kidney), and an abscess is pointing under Poupart's ligament with acute symptoms of febrile disturbance, the speedy evacuation of the pus is indicated likewise. On the other hand, the more chronic forms of abscess connected with caries of the vertebræ or pelvic bones should be left to themselves as long as possible, owing to the danger of letting in air and setting up decomposition. The proper way of opening such abscesses, and the necessary precautions, are fully described in books on surgery.

Care should always be taken, when the disease runs a more sluggish course, to rectify the malposition of the limb by gradually extending the muscle, and fixing the thigh in its improved attitude.

GOUT.

The literature of gout is so very rich that I find it impossible to do more than mention a few of the works on the subject. Some are referred to in the bibliographical introductions to the sections on the rheumatic affections of the joints and muscles.—*Hippocrates*, De affect. int. lib. VII. Aphorism. VI. 9, 28–30, etc.—*Celsus*, De medicinâ. IV. 1.—*Caelius Aurelianus*, De morb. chron. V. 2.—*Rufus Ephesius*, De podagra.—*Paulus Aegineta*, III. 78.—*Demetrius Pepagomenus*, De Podagra. Lugd. Batav. 1743.—*Hemsterhuys*, Historia anthritidis vagae. 1666.—*Sydenham*, Tract. de podagra et hydrope; and Processus integri in morbis, etc.—*W. Musgrave*, De Arthritide sympt. Londini, 1703. De Arthritide anomala. Diss. Oxon. 1707. De Arthritide primigenia et regulari. Op. posthum. Londini, 1756.—*Morgagni*, Epistol. LVII.—*C. L. Liger*, Traité de la goutte. Paris, 1753.—*Boerhaave*, Aphorism. 1254 *seq.*—*Fr. Hoffmann*, Med. rat. syst. de dolore podagrico et arthritico, de podagrâ retrocedente in corpus, etc.—*Ferd. Warner's* Description of the Gout.—*W. Cadogan*, Treatise on the Gout and other chronic maladies. 1770.—*W. Falconer's* Observations on Cadogan's treatise. 1772.—*Forbes*, Treatise on Gout and Gravel. London, 1793.—*J. Parkinson*, Observations on the nature and cure of gout. London, 1805.—*P. J. Barthez*, Traité des maladies goutteuses. 1805.—*A. P. Wilson*, Treatise on inflammations, rheumatism, and gout. 1807.—*Th. Sutton*, Tracts on delirium tremens, gout, etc.—London, 1813.—*E. Scudamore*, A treatise on the nature and cure of gout. London, 1816.—*St. Ursin*, Etiologie et thérapeutique de l'arthritis et du calcul, ou opinion nouvelle, etc. Paris, 1817.—*C. A. Meyer*, Versuch einer neuen Darstellung des Unterschiedes zwischen Gicht und Rheumatismus. Hannover, 1820.—*Cadet de Vaux*, De la goutte et du rhumatisme. 1820.—*L. A. Tuerck*, Traité de la Goutte. Paris and Nancy, 1837.—*Duringe*, Monographie de la Goutte.—*Graves*, Clinical Medicine. 1843. Lecture 37.—*W. Budd*, Researches on Gout. Med. Chir. Trans. XXXVIII. 234.—*Joh. Wendt*, Die Gicht, ihre Zufälle, etc. Breslau, 1844.—*Alex. Ure*, London Med. Gazette, November, 1844.—*Bence Jones*, On Gravel, Calculus, and Gout.—*Bramson*, in Henle and Pfeuffer's Ztschrft. für rat. Med. 1845. III. 175.—*Wilson*, Observations on gout and rheumatism. London, 1848.—*Garrod*, Researches on Gout, in Med. Chir. Trans. 1848. XXV. 83; 1854. XXXVII. 49. On the Nature and Treatment of Gout and Rheumatic Gout. 3d. edition. 1876.—*W. Gairdner*, On

Gout.—*J. Alexander*, Rheumatism, its nature, cause, and cure; gout, its nature, etc. London, 1858.—*Braun*, Beiträge zu einer Monographie der Gicht. Wiesbaden, 1860.—*Roth*, Das Vorkommen der Gicht in der Cur zu Wiesbaden. Virchow's Archiv. XXVII. 1. — *Trousseau*, Clinical Lectures (Sydenham Society's translation).—*Charcot*, Du rhumatisme noueux et de la goutte. Gazette des hôpitaux. 1866. 80; 1867, 12 *seq.*—*C. Hueter*, Klinik der Gelenkkrankheiten. Leipzig. 1871, p. 111, 346 *seq.*—*Meldon*, A new theory of gout, in Lancet, 1872, July 27; also, A treatise on gout, rheumatism, and rheumatic gout. London, 1873.—Also innumerable papers in various periodicals.

Historical Introduction.

Gout (arthritis uratica, s. urica, s. vera, panarthritis urica [Hueter]; or simply arthritis; also podagra) is a chronic constitutional disorder, occurring in paroxysms attended with pain, during which salts of uric acid are deposited chiefly in and around the joints or in other cartilaginous structures.

Our knowledge of this disease dates from the most remote antiquity. It would appear, from frequent notices both in medical and non-medical literature (Lucian, Seneca), to have been far more common than it is at present in Greece and Italy, especially amid the wealth and luxury of the Roman Empire. In our day it is most common in England.

The oldest medical writers described gout among diseases of the joints, in immediate connection with "rheumatic" joint-affections. But even later authors, while distinguishing between gout and rheumatism, regarded them as closely related to each other,—as divers manifestations of the same constitutional state —the "gouty-rheumatic diathesis," a view which has held its own into the present century. This diathesis was held, from the time of Hippocrates downward, to consist essentially in a morbid state of the humors, variously interpreted, in conformity with changes in the prevalent humoralism, as a metastasis of the "humores cocti," or of the mucus and the bile, or of an atrabiliary humor; subsequently, as an accumulation of earthy particles; lastly, after Wollaston (1797),[1] Tennant, Fourcroy, and others, had proved that uric acid was the chief constituent of gouty deposits—as an accumulation of uric acid in the system, a "uric-acid dyscrasia." How this last condition was brought about, and what the nature of its connection with the symptoms of gout might be, are questions that still remain unsettled; many writers, as Boerhaave, Sutton, and of late years Todd and Gairdner, regard digestive anomalies as the primary mischief, causing the blood to become loaded with uric acid and other excretory products; others, again, agree with Garrod in laying stress chiefly on a disturbance in the function of the kidneys, leading to an impure condition of the blood. The view of the solidists, represented by Cullen, who considered gout to be an affection of the nervous system, has never been able to hold its ground against the various humoralistic theories alluded to above.

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[1] On gout and urinary concretions. Philosoph. Trans. 1797. II. 386.

If we put aside the theories of the older physicians, we shall find their descriptions of gout to be so pointed and complete as to leave no room for improvement. The picture they drew has often been obscured, however, by the way they had of regarding any and every disease of internal organs as a manifestation of the gouty diathesis (latent, internal, anomalous, or retrocedent gout). The connection between the diathesis and its manifestation was based on a few very doubtful indications, and could never be demonstrated. Sydenham's description of gout is still the best we have; he supplemented his extensive knowledge of the disease in others by personal experience. Musgrave may be taken as a representative authority on the various forms of "anomalous" or "irregular" gout. And it is to English physicians that we are indebted for whatever progress has been made of recent years in our knowledge of this disease.

Etiology.

Hereditary predisposition may be shown to exist in the vast majority of all cases of gout. Scudamore[1] found that thirty-four out of seventy-seven gouty patients came of gouty parents; Gairdner's proportion amounts to 140 out of 156. Among his hospital patients, Garrod found one-half with a hereditary predisposition, while Braun, in his practice at Wiesbaden, did not find one among his sixty-five patients whose parents or grandparents had not suffered from the disease. The tendency is much more frequently derived from the father's than from the mother's side, probably because women are much less liable to gout than men, and do not usually begin to suffer from it till after the period of sexual fertility is over. The predisposition may often be traced to the grandparents, while the parents, especially if they avoided the exciting causes of the gouty paroxysms, remained free. In some families the inherited tendency is so strong that all their members, whatever precautions they may adopt, suffer from gout; and in many English families the disease has been handed down from father to son for centuries (Garrod).

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[1] These and other statements of *Scudamore's* are quoted from *Hasse's* German edition of his works. The figures quoted by *Canstatt*, *J. Vogel*, *Braun*, (in his translation of *Gairdner's* book), and others, are different; I have not been able to trace the difference to its source. They make *Scudamore* find 105 cases of gout with a hereditary tendency among 189, while *Braun's* monograph gives the figures as 331 among 522.

Next in importance to hereditary predisposition stands the patient's own mode of life. This may bring on gout without any help from inheritance. Gout has long been recognized as a disease of the wealthy, as a result of luxury and intemperance, of the immoderate use of animal food, highly-seasoned dishes, heady wine and beer, combined with sedentary habits.[1] Whether the abuse of intoxicating beverages is capable, by itself, of originating gout, may be doubted, especially as the disease is comparatively rare among the poorer class—the class which furnishes the greatest proportion of habitual drunkards. It is to the joint operation of two or more of the causes enumerated above that we must ascribe the greater prevalence of gout among dwellers in cities than among country-folk, among learned men and statesmen than among the laboring people. Hence, too, the curious fact that gout not unfrequently disappears, after having lasted for years, when the patient's mode of life undergoes a sudden change (as from loss of fortune, want, anxiety, etc.). As Sydenham says: "Articularis hicce morbus, quod mihi aliisque solatio esse possit, divites plures interemit quam pauperes, plures sapientes quam fatuos, etc." The prevalence of gout in England and northern countries generally (especially Holland) is explained by the custom of dining freely, and washing down large quantities of animal food with profuse libations of strong drink; its rarity in Italy and southern Europe, by the habitual moderation exercised in the matter of food and drink.

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[1] The ancients looked on gout as the daughter of Bacchus and Venus. There is an old rhyme which runs thus:

"Vinum der Vater, Cœna die Mutter,
Venus die Hebamm' machen das Podagram."

The male is far more liable to gout than the female sex. This is principally due to the fact that women are usually more abstemious in their use of alcoholic liquors, and less given to sexual excesses than men. The authority of Hippocrates (Aphorism 29, Sect. VI.) gave currency to the notion that women were protected against gout by menstruation, and were only attacked by it when this function was interfered with, or after the climacteric period; but this rule has been found to be far from universal, and the belief which formerly prevailed in the depurating effect of the menstrual flow on the system has long since been given up. It is quite possible, however, that those causes by which the menstrual function is disturbed may promote the occurrence of gout, and *vice versa*. It should always be borne in mind that gout is undoubtedly more common in women of mature age.

Age is a great element in determining the outbreak of the malady. Gout usually makes its first appearance between thirty and forty; sooner in persons with a hereditary than in those with an acquired tendency. Occasionally, when inherited predisposition happens to coincide with that due to habits and regimen, we find the disease breaking out at an earlier period—during youth, or even, if we are to believe the statements of many writers, in childhood.

Scudamore furnishes the following statistics, based on the observation of 64 cases: the first attack of gout occurred between the 20th and 25th years in 6; between 25 and 30 in 17; between 30 and 35 in 14; between 35 and 40 in 13; between 40 and 45 in 2; between 45 and 50 in 6; between 50 and 55 in 2; between 55 and 60 in 3; between 60 and 65 in 1. Sydenham, Heberden, Garrod, and others state that they have never seen gout occur before the age of puberty. Gairdner, on the other hand, has seen more than one paroxysm of regular gout even in infants at the breast. Trousseau met with it in a boy aged six, and Debout (Union médic. 1869. No. 103) in several children between ten and fifteen years of age. Some of the older writers on medicine (Aretaeus, Morgagni, etc.) also allude to the occurrence of gout in children; but they may have confounded true gout with rheumarthritis.

There is yet another cause capable of originating gout, even without the aid of inherited predisposition. I allude to the prolonged influence of lead, which was noticed casually by Musgrave and Parry (1807); but special attention was first drawn to it by Garrod and Charcot (Gaz. hebdom. 1863. 27). Their experience has been confirmed by others,[1] and amounts to this: that cases of gout—which, as already stated, is decidedly uncommon among the laboring poor—are chiefly met with in this class of patients among persons who have a great deal to do with lead (house-painters, lacquerers, type-founders, workmen in lead-mills, etc.), and who have already suffered from colic or other symptoms of chronic poisoning by lead; so that a direct connection between gout and the saturnine cachexia must be admitted to exist.

The exciting causes which bring on the individual paroxysm in persons with an acquired or inherited tendency to gout are very various: exposure to cold and wet, errors of diet, sexual excesses, violent outbursts of passion; not unfrequently, too, mechanical injuries, such as knocks and bruises, or concussion of the whole body; sudden changes of regimen, etc. Change of weather exerts a powerful influence; north and east winds are especially dreaded by gouty people, paroxysms of the disease being most frequent in spring and autumn.

Pathology.

The characteristic feature of gout is the peculiar, periodic recurrence of the joint-affection—the gouty paroxysm. But it may call forth a variety of other disorders in internal organs, which may exhibit either a periodic or a continuous type; these disorders may set in from the first, or they may, and usually do, defer their appearance till after the patient has gone through a series of attacks of regular gout. These various manifestations of the disease are commonly distinguished as particular forms of it. Cullen, for example, is followed by many writers in separating from the proper gouty paroxysm (normal, regular, true, acute gout) an atonic form (torpid, chronic gout), a retrocedent form, and an aberrant form (internal, latent, masked, metastatic, anomalous gout). Others, again, are content with a division into regular and irregular gout, including under the latter term all those gouty troubles which do not assume the form of the complete paroxysm.

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[1] *Bricheteau*, Gazette des Hôpitaux, 1870, 26. *Bucquoy*, Union Méd., 1868, 74. *Wilks*, Guy's Hospital Reports, 1870, XV., p. 40.

These diversities are principally due to the fact that when the disease has lasted a long time, or when the patient's constitution is worn out, profounder changes begin to be wrought in the system. These deeper changes no longer subside as completely as the earlier paroxysms, when the patient's constitution was still unimpaired, and other circumstances were more favorable to recovery. The typical form of regular gout, with its intervals of apparently perfect health, is thus obscured; the joint-affection grows more chronic, other organic mischief comes gradually to the fore, and the patient ultimately passes into a state of disablement which only recalls the earlier type of the disease by its alternate exacerbations and remissions.

All these varieties, and especially the typical or genuine form of gout, are usually preceded by a long period of incubation lasting for months or years. Taken by itself, this period offers little to indicate its true significance. The patient suffers from all sorts of trouble in his abdominal viscera, trouble usually included under the elastic term "abdominal plethora," and mainly caused by the mode of life described above, viz., a liberal dietary, a free use of wine and beer, and insufficient bodily exercise. Such patients usually complain of indigestion in all its forms; tension and fullness of the epigastrium, tympanites, retching, and heart-burn, irregularity of the bowels, with a tendency to constipation; the urine is often scanty for days together, highly concentrated, scalding the urethra, and depositing a sediment of urates soon after it is passed. These symptoms are often associated with hemorrhoidal troubles, depression of spirits and irritability, hypochondria, palpitation of the heart, præcordial anxiety, sleeplessness, etc. The gouty proclivities of many such patients are manifest at a glance: they are corpulent, their complexion is livid, with a shade of yellow, and their nose red at the tip (*Acne rosacea*). I need hardly add that this state of things does not invariably end in gout; while, on the other hand, there are many gouty subjects, especially among those with an inherited tendency, who do not present the appearance I have just described.

A.—Regular or Typical Gout. The Normal or Acute Gouty Paroxysm. (Podagra.)

The seizure is almost always preceded by warning symptoms. These are extremely various and indefinite. Sometimes they consist in disturbances of digestion, in an exacerbation of the patient's gastric troubles; sometimes in nervous symptoms, such as restlessness, uncertainty of spirits, a sense of weariness, or painful dragging of the limbs; sometimes in definite pyrexial phenomena, such as alternate shivering and heat of skin, with perspiration; sometimes, again, the patient may feel exceptionally brisk, in unusually high spirits, with an increased appetite, etc. As a general rule, the same patient always experiences the same premonitory symptoms; so that a man who has already suffered once, or more than once, is often aware of the approach of a fresh attack, while, on the first occasion, he is usually taken at unawares. The premonitory symptoms may last from a few hours to several days.

Graves says that in hereditary gout the symptoms premonitory of the first attack are often very slight, increasing progressively in their severity as the attacks recur; whereas, in acquired gout, they exhibit an inverse order of intensity.

The actual seizure usually occurs during the night, between midnight and three A.M. The patient is suddenly aroused by acute pain in the affected joint, usually (when the disease is recent) the metatarso-phalangeal joint of one great toe. He feels as though a nail were being driven into the joint, or as though the toe were being crushed in a vice, or bored with a red-hot iron ; the slightest touch causes agony ; the limb is often affected by twitchings which add to the patient's sufferings. The pain continues unabated till dawn, when the affected part is found to be swollen, the skin over it reddened, hot, dry, and glazed, the neighboring veins more prominent than usual. The patient is feverish ; a brief rigor is followed by heat of skin, a quick, full, compressible pulse, and a scanty secretion of urine of high specific gravity, depositing an abundant sediment. Towards morning the pain at last abates, the local symptoms and the fever subside in some degree, the patient breaks out into a perspiration, and obtains some of the rest for which he craves. The day is spent in tolerable comfort ; the joint continues to be red and swollen, though less hot and tender ; the neighboring skin is more or less œdematous.

But on the ensuing night the same scene is repeated. All the phenomena of the paroxysm recur, perhaps with less violence, and subside again towards morning. This goes on for about a week or ten days, every night witnessing an exacerbation, every day a remission of the symptoms. The first attack seldom lasts for less than five or for more than ten days. By the third or fourth night the symptoms have grown much milder ; finally the swelling entirely subsides, the skin resumes its normal hue, the cuticle peels off in flakes, the dilated veins disappear. The affected region continues for several days to be unusually sensitive and stiff—this feeling of stiffness lasting longer in old people and those who have suffered repeatedly before. The patient soon regains his health ; nay, he feels like a new man after the sufferings and sleepless nights that he has gone through ; many patients, especially the younger ones, profess to feel decidedly better, after their first attack of gout, than they felt before. The duration of the paroxysm usually stands in an inverse ratio to the severity of the pain, the degree of restlessness, excitement, and fever. The converse holds good likewise.

It is only in a few exceptional cases that the first attack of gout is also the last. As a rule, the disease recurs, under favorable circumstances, at intervals of many months or years ; when the patient's habits and inherited tendencies are against him, at intervals which are much shorter. The length of the interval is usually proportionate to the violence of the foregoing attack.

The first paroxysm commonly occurs towards the end of winter or the beginning of spring; the subsequent ones, either at the same season, or in autumn too; not unfrequently at regular annual or biennial intervals.

In nearly three-fourths of the total number of cases, the first attack is limited to the metatarso-phalangeal joint of one great toe, the left toe being apparently more often chosen than the right (Gairdner); in a small minority of cases both great toes are involved at once, or the ankles, or some other joint in the foot. To the first attack, therefore, the term *Podagra*, "foot-gout," is peculiarly applicable. Other joints, as *e. g.*, those of the hands (*Chiragra*), or the knee (*Gonagra*), are very rarely the seat of a first seizure; and even when they are, the foot is usually attacked with them. The shoulder-joint (*Omagra*), the elbow, the hip (*Ischiagra*), the intervertebral joints (*Rhachisagra*), and other articulations, are only involved in very old cases of the disease, simultaneously with the feet.

The following is the proportion between the various joints affected in a first attack of gout, as observed by Scudamore in a series of 71 cases. One great toe was attacked in 49, both great toes in 4, one great toe together with the inner aspect of the foot in 2, the outer aspect of one foot in 2, one ankle-joint in 2, both ankle-joints in 1, one ankle-joint with the inner aspect of the same foot in 1, one great toe together with the inner side of the foot and the ankle-joint in 1, the inner aspect of both feet in 1, the heel of one foot in 1, both feet and both hands in 1, one toe and one thumb in 1, the right knee-joint in 1, the left knee in 1, the back of one hand in 1, one wrist in 1, the backs of both hands in 1. Garrod found that only in 5 out of 100 first seizures were any joints besides the great toes affected. Braun (in his translation of Gairdner's work) gives a summary of 28 first seizures; in 24 of these one great toe was attacked, in 2 the dorsum of the foot, in 1 the knee-joint, and in 1 the hand.

The severity of the individual symptoms abates with each successive paroxysm of gout; but the paroxysms themselves last longer, and may drag on for two or three weeks, or even a month. Subsequent attacks are no longer confined to the joint originally affected, but involve others either simultaneously or alternately; sometimes the disease may shift from joint to joint (*Arthritis vaga*). Then, too, the local phenomena are less and less disposed to subside completely; the skin remains reddened and traversed by varicose veins; the swelling no longer subsides as completely as it did, but rather exhibits an increase after every fresh attack; the constitutional symptoms show less tendency to disappear, the patient no longer finding himself free from his sufferings in the intervals between successive paroxysms; in short, the disease gradually becomes chronic. At the same time the individual attacks lose their definite and typical character; the organism seems no longer able to bring forth a sharp attack of acute gout, or—on the view of the ancient physicians—to expel the *materies morbi* from the blood by a vigorous effort at elimination. Hence the name "atonic gout" applied to the malady at this stage.

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B.—Irregular, Chronic, Atonic Gout.

In the vast majority of cases, this variety of gout is evolved from the typical form, when the latter has persisted for many consecutive years. We find it chiefly in older people, whose strength has been more or less undermined by age and long ill-health and by the continual recurrence of gastric disorder. Unsuitable treatment of the earlier attacks, such as the abuse of narcotics or blood-letting, is said to favor the transition from the regular to the irregular and chronic form of gout. Sometimes, but far more rarely, the disease is chronic from the beginning; this is most likely to happen in sickly women with a strong inherited proclivity.

The chronic variety of gout contrasts with its acute form by the diminished intensity of the articular inflammation and the greater prominence of the attendant disturbances. The prodromata are much more definite and prolonged. The patient is tormented, for days together, by dyspeptic symptoms of all sorts; his tongue is thickly coated; he has pain in the epigastrium, his abdomen is tumid, he suffers from colic and diarrhœa, frequent sweating, and marked variations in the quantity and quality of the urinary secretion, which is generally pale, clear, and of low specific gravity. His temper is depressed, irritable, and quick to anger.

The onset of the paroxysms is no longer exclusively nocturnal. They may be brought on at any hour by trifling or accidental causes, and are no longer attended by the old agonizing pain, high fever, vivid redness and heat of the joints. The tenderness is much less marked; heat and swelling come on slowly and imperfectly; the febrile movement is slight, or may be wholly absent. The digestive troubles, on the other hand, persist with undiminished intensity; vague pains are felt elsewhere, by which the patient is often more annoyed than he is by the joint-affection. Some of these symptoms gradually subside; but the local swellings are not entirely dispersed; a soft, doughy, or even fluctuating tumor remains behind, which is due to an exudation, rich in urates, either into the joint itself, or into the tissues around it. The sparingly soluble urates are left when the exuded liquid is reabsorbed; the joint does not regain its former mobility, and the patient misses the general sense of relief and well-being which used to follow a typical paroxysm of the disease. Digestion is permanently out of order, and he finds walking exercise troublesome.

After a succession of these attacks, the joints become permanently distorted, nodulated, or fusiform; the bones are often dislocated. The swollen parts feel pasty or gritty to the finger, and at last become quite hard. These swellings—the so-called tophi or gouty concretions (*nodi arthritici*)—are most commonly situated on the joints of the hands and feet, on the tendons of the fingers and toes, and on the elbow; they may reach the size of a walnut.

In cases so far advanced as these, concretions may also form in parts distant from any joint; their formation may coincide with a paroxysm or may be attended with pain, or it may occur during an interval, without the patient being aware of it. The most common seat of such deposits is the ear, where they attain the size of a pin's head or even of a pea; they are also met with elsewhere, in the subcutaneous connective tissue, in the nasal and tarsal cartilages, in the muscles and their tendons.[1] Old writers give cases in which the entire body was studded with such concretions.

The veins are seen to be much dilated and varicose in the neighborhood of the swollen and encrusted joints; they may not unfrequently be traced as hard cords to some distance along the affected limb. Paget[2] points out that they are usually filled with blood-clot, and may give rise to embolism.

Chalk-stones of limited size, and not of very old standing, may become absorbed and disappear under appropriate management. But after they have remained *in situ* for any length of time and have increased in size, they act as foreign bodies and set up irritation. The skin over them becomes inflamed and finally gives way under circumstances of considerable suffering. The abscess thus produced discharges a milky paste or mortar-like material, consisting of pus mixed with urates; or else a thinner and more sanious liquid, holding larger particles in suspension, which sometimes stick to the edges and base of the ulcer, and look like stalactites. The ulcer itself is indolent, and looks spongy and relaxed; it shows little tendency to heal; even if it closes up, a trifle is enough to open it afresh. When an abscess of this sort has burst and set free its contents, the affected part not unfrequently becomes less painful, and regains its former suppleness in some degree. When they are numerous and chronic, however, the ulcers only contribute to wear out the patient's strength and hasten his dissolution.

The disease often drags along in this way with alternate exacerbations and remissions till its final issue. The patient usually feels better during the summer months; a temporary respite may be gained by an altered mode of life and suitable treatment; but as the inclement season of the year comes round, the malady resumes its virulence, and exacerbations which remind us of typical gouty paroxysms set in once more. The joints are permanently swollen, the digestion is always out of order, the state of the patient's nutrition grows steadily worse, and a general enfeeblement of the system becomes associated with the pain due to movement of the stiffened and distorted joints. The patient shuffles wearily about with the help of a stick; or else, avoiding all exertion, he cowers, peevish and morose, wrapped up in blankets and feather-beds, morbidly alive to external influences, dreading every change of weather, every draught of air, etc. The skin is inclined to perspire, and owing partly to this cause, partly to constitutional cachexia, falls a prey to divers eruptions. The patient is further tormented by vague nervous symptoms, such as wandering pains, palpitation of the heart, præcordial anxiety, singing in the ears, etc., without any demonstrable organic lesion to account for any of them.

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[1] *Wyss* asserts that the tophi situated in the skin originate in the sudoriparous glands. (Memorabilien für Prakt. Aerzte, 1870, p. 233.)

[2] St. Bartholomew's Hosp. Reports, 1866. II. p. 82.

In many cases, again, we have complications of another kind, viz., acute or chronic affections of internal organs, grouped under the common head of "visceral" or "internal" gout, when a causal connection is suspected to exist between them and the gouty paroxysm, or when they are regarded as manifestations of the gouty diathesis. There is scarcely any disease which has not been called "gouty" in this sense of the word; many of the older physicians, indeed, laid themselves open to the charge of exaggeration by ascribing a specifically gouty character to every malady, no matter what, occurring in persons either actually subject to gout, or simply predisposed to it. On the other hand, we must beware of running too far into the opposite extreme, like some modern writers who absolutely reject all belief in any connection between gout and certain diseases of internal organs. It is perfectly true that we sometimes find gouty subjects afflicted with diseases whose course and symptoms betray their intimate connection (if we take them as a whole) with the gouty affection of the joints, their causal dependence on the same diathesis. Anatomically, the gouty nature of such internal disorders can only be proved by finding the same deposits of urates as those which characterize the joint-affection itself. Hitherto, however, apart from a few rare and exceptional cases, we only know of one instance in which this proof has been furnished. Garrod has shown that there exists a form of renal disease associated with the precipitation of urates in the parenchyma of the kidneys, and which may therefore be legitimately viewed as a gouty nephritis or *nephritis uratica*, like the equally common *pyelitis uratica*. These affections of the kidneys differ but little, as regards their symptoms, from the chronic forms of diffuse nephritis arising in other ways ; indeed, a nephritis or pyelitis uratica can hardly be distinguished from other forms of nephritis and pyelitis, except by finding an excessive amount of urates eliminated in the urine. Apart from this condition of the urine, there exists no specific symptom capable of indicating the gouty character of any visceral disease. It is only when a particular malady deviates from its usual course by suddenly receding as the characteristic joint-affection breaks out, or by breaking out when the latter subsides, that we are justified in regarding it as probably of a gouty nature. Cases of the latter kind have been termed "retrocedent" or "metastatic" gout, on the supposition that the *materies morbi*, deserting the joints, transfers itself to other parts, where it sets up irritation. Cases of the former kind, where an internal disease of importance, after obstinately resisting all treatment, stops abruptly when the typical paroxysm of gout sets in, are termed cases of "masked" or "latent" gout. So long, however, as no such alternation has occurred, we are not justified, however unusual the symptoms may be, in doing more than suspect the existence of latent gout, even in persons with an undoubted predisposition to the disease, or who have already suffered from it. Our suspicions may receive support from the favorable issue of some mode of treatment regarded as specific.

There is a group of external disorders of a painful kind, distinct from the articular disorder, which may, with some degree of assurance, be regarded as of gouty origin, when they happen to be associated with deposits of urates. Such deposits are occasionally met with under the scalp, in the connective tissue, or in the muscular and aponeurotic coverings of the skull ; they cause very severe pain, which may fairly be designated "gout in the head" or "gouty migraine." In other cases, which have been described under the name of "neuropathic gout," the seemingly neuralgic paroxysms may really be due to similar deposits in the periosteum or in the muscles of the trunk and limbs. It is possible that similar deposits may occur in the intervertebral joints, and cause neuralgic symptoms by irritating the nerves at their exit from the vertebral canal ; but it is more likely that such symptoms, occurring as they mostly do in oldish people, are indicative of chronic inflammatory processes developed as independent complications of true gout.[1] Taken altogether, the number of cases that can fairly be regarded as "visceral gout" is very small. Most of the affections described under this name, especially by the older writers on this subject, are either *sequelæ* of gout (due to absence of exercise, being cooped up in hot, ill-ventilated rooms, and other conditions favorable to venous congestion, and fostering a liability to catarrh, etc.), or else *complications*.

The predisposing causes of gout, viz., habitual over-indulgence in heavy meals and alcoholic beverages, sexual excesses, want of exercise, etc., tend also to bring on a variety of other disorders, which are, for this very reason, often met with in association with gout. Though related to this disease, they cannot fairly be regarded as manifestations of the specific gouty diathesis. Nevertheless, they are often viewed in this light. A host of abdominal disorders and hemorrhoidal troubles, various affections of the liver and stomach, renal and biliary calculi, with other chronic diseases of the kidneys and bladder, are often due to causes enumerated above, and are accordingly often met with as complications of gout. The cerebral and cardiac symptoms, more especially the apoplexies, fainting-fits, anginal paroxysms, pulmonary congestions, so often met with in gouty patients at an advanced stage of the disease, and whose suddenness of onset and rapid course naturally lead to the belief in abrupt metastasis, ought almost always to be ascribed, not to specific gouty changes in the heart and blood-vessels, but to chronic endo-arteritis of the cerebral and coronary arteries, with its usual consequences—a disease which is common enough apart from gout. The atheromatous degeneration, and especially the calcification of the arterial walls found in such cases, are often regarded, when they are present in gouty persons, as analogues of the articular deposits—as internal chalk-stones; but this view could only be maintained with justice if the structural changes in question were found to coexist with an excess of urates, and no such excess has, up to the present time, been demonstrated.

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[1] Such is, in all probability, the correct interpretation of many cases recorded by *Albers* (Deutsche Klinik, 1849. No. 25); they ought to be regarded as instances of *Spondylitis deformans* (Vide *Arthritis deformans*) occurring in gouty subjects.

Anatomy and Chemistry.

The one structural change constantly found in the bodies of gouty patients who have at last succumbed to their protracted sufferings is the change in those joints which were the seat of the disease during life. This change consists in the deposit of a material, chiefly made up of urates with a very minute proportion of organic matter, in the articular tissues, and—in very old cases—in the peri-articular tissues as well, *sc.* in the *bursæ mucosæ*, the sheaths of tendons, and even in the periosteum of the epiphyses. First and most frequently, we find the articular cartilages, the fibrous capsule, and the synovial membrane, encrusted with a white or yellowish-white material resembling sand or plaster-of-Paris. Budd says that the central part of each disk of cartilage is most abundantly impregnated, the proportion of the foreign matter diminishing towards its edges, so that the zone lying next to the synovial capillary network may appear quite unaltered. Budd's researches, confirmed by those of Cornil and Ranvier, indicate the cartilage-capsules as the centre and starting-point of the deposits. They first of all become crowded with tufts of crystals; similar tufts then make their appearance in the intercellular matrix. In marked contrast to this arrangement Zalesky found that the deposit of urates, artificially produced in birds by ligature of the ureters, occurred primarily in the intercellular substance. The chief constituent of the deposits is acid urate of soda; next comes sodic chloride, and compounds of uric acid with lime, magnesia, and ammonia. Carbonate and phosphate of lime are not unfrequently present, and Budd even detected hippuric acid.

According to Garrod, the following is the way in which the urates are deposited: A tolerably clear, transparent liquid is first of all effused into the tissues; out of this fluid the salts enumerated above crystallize; they remain after the fluid portion of the exudation has been absorbed.

Besides these deposits we find more or less distinct traces of inflammation in and about the joint. These are due to a mechanical or possibly even chemical irritation set up by the deposited urates, and consist of hyperæmia and thickening of the synovial membrane, œdema of the peri-articular connective tissue, dissociation and fraying-out of the cartilage, and sometimes even caries of the epiphyses, ankylosis, dislocation, etc.

As already stated, the deposits may occur in other superficial parts as well as in the joints; nay, we find cases on record in which urates were discovered in the cancellous tissue of the bones (Monro, Cruveilhier, Fauconneau-Dufresne, Virchow[1]). They might probably be found in internal parts more frequently than they are, if post-mortem examinations of gouty subjects were more common. Hitherto, if we set aside the renal infarctions presently to be described, only two facts of the kind have been recorded. Virchow discovered a chalk-stone in the larynx, and Liger asserts that he has met with them in the lungs.

Of all internal organs the kidneys are most often the seat of structural change. The change usually consists in granular atrophy, at any rate in old cases of gout; the organ is shrivelled, with a rough, granular surface, a thickened and adherent capsule; on section, the cortex is seen to be shrunken, tough, and uneven. In very advanced cases, we find the deposits of urates described by Garrod. The urates form whitish streaks, extending from the pyramids and the medullary substance into the cortex; the granular, amorphous deposit is first of all confined to the uriniferous tubes and their epithelium; at a later stage, it extends into the interstitial tissue likewise, where it often assumes the form of stellate crystals. In many cases we also find a catarrhal pyelitis due to the irritant effect of the gravel or of larger concretions.

The body, moreover, commonly shows signs—apart from the traces left by intercurrent disease—of one or more of the visceral complications previously alluded to; I refer more especially to atheromatous and calcareous changes in the arteries, and other organic lesions of a senile type.

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[1] Archiv für path. Anat. XLIV. p. 137.

I have already pointed out that the calcareous deposits in the walls of the vessels ought not to be mistaken for true gouty concretions similar to those in the joints. Still, it is quite possible that in individual cases of gout, uric acid may enter into their composition. Schroeder van der Kolk,[1] in dissecting a hand studded with chalk-stones, found the neighboring veins thoroughly impregnated with urate of lime, and looking like white cords.

The blood of gouty patients was suspected by Forbes, Jahn, and Rayer, to contain urate of soda in excess; but Garrod was the first to demonstrate its presence. According to this author, the blood in gout contains at least .025 to .175 parts *per mille* of uric acid, whereas in health and in many other diseases it has been shown to contain mere traces of this salt.

We know nothing more, with any certainty, about the state of the blood. Garrod says the proportion of fibrin is increased during the gouty paroxysm. The same observer has found an excess of uric acid in the fluids transuded into the pericardium and peritoneum, and in the serum of blisters.

The method employed by Garrod for determining the presence of uric acid in the blood is known as the thread-test. It only yields positive results when a large excess of the acid is present, and allows of nothing more than an approximative estimate of quantity; but it is valuable on account of the ease with which it may be applied. From half an ounce to an ounce of freshly-drawn blood is allowed to coagulate, and about 10 c.c. of the serum poured into a shallow watch-glass about three inches in diameter; ordinary acetic acid (containing about thirty per cent. of the pure acid) is then added in the proportion of one to ten, and a fine, rough thread, about an inch in length, plunged into the mixture. The watch-glass is then set aside in a moderately warm place for from twenty-four to forty-eight hours and protected from dust. If the serum contain a minimum proportion of .025 *per mille* of uric acid, the latter will crystallize out upon the thread in the form of delicate rhombic crystals recognizable under the microscope.

Uric acid has long been known to exist, and has often been demonstrated, in the perspiration of gouty patients (Swediaur, Mayer, Bird, Charles Petit, Chomel, Garrod). But it is not invariably present de Martini and Ubaldini[1]). Possibly its presence may give rise to the formation of chalk-stones in the skin.

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[1] Nederl. Lancet. 1856, July and August, p. 97.

Vigla's assertion,[2] that in gout and the uric acid diathesis the saliva is acid, deserves no credit, for it really refers to the mixed liquids in the buccal cavity, which, as everybody knows, may vary widely in their reaction.

The state of the urine in gouty patients is of the highest interest. Fromherz and Gugert, Jahn, Prout, Berthollet, had all of them observed a diminution in the quantity of uric acid ; in regular gout this diminution was only observed before each paroxysm ; in chronic gout it was found to be constant. But all these observations were vitiated by a fundamental error. Garrod was the first to obtain trustworthy data concerning the changes in the state of the urine associated with the different stages of the disease ; and his results have, in the main, been confirmed by subsequent inquirers (C. G. Lehmann, Ranke, Braun). The following are the conclusions that have been arrived at : in typical acute gout the proportion of uric acid in the urine undergoes a marked decrease several days before the paroxysm ; it may fall to one-half or less of the normal daily quantity. During the paroxysm—at least during the first few days—but little uric acid is excreted ; its quantity sinks even lower than it had sunk before ; it then rises once more, so that, towards the close of the attack, it may be regarded as relatively normal. It is quite true that the usual average is not always reached ; but then we must take into account the low diet on which the patient has been kept, and the occurrence of other evacuations. Berthollet[3] and Scudamore state that the proportion of phosphoric acid in the urine is markedly augmented during the attack. The other constituents of the urine do not present any considerable deviation from the average during a typical paroxysm. The total amount of the secretion is, as I have already observed, diminished ; it does not return to its usual average till the paroxysm is on the decline. In the intervals between the attacks of regular gout the urine is often found to be poor in uric acid; upon the whole, however, its condition in this respect may vary widely, and may continue normal for long periods of time.

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[1] Presse médicale belge. 1866. XVIII., No. 6.

[2] Gazette des Hôpitaux, 1872, No. 27.

[3] Quoted by *Scudamore*, loc. cit. S. 84 ff.

As the disease becomes chronic, and the paroxysms lose their typical character, the difference between the state of the urine during and between the paroxysms—especially as regards the proportion of uric acid—becomes gradually less appreciable. The urine is generally paler and less highly concentrated; its quantity varies according to the food and drink taken, and the same may be said of its principal constituents, with the exception of the uric acid. This is always diminished, and may be reduced to a mere trace, scarcely admitting of quantitative determination. In old cases, when the digestion is much disturbed, oxalate of lime often makes its appearance in considerable quantity, forming a sediment (Prout, Begbie, Rayer, Gallois); many observers have also detected sugar (Prout, Lehmann, Gairdner), though always in small proportion and as a temporary phenomenon. For my own part, I have never succeeded in finding a trace of sugar in several cases of very chronic gout. Finally, as the cachexia grows more profound, the urine often assumes a character indicative of contracted kidneys: it is very copious, pale, deposits a trifling sediment, or none at all, is of very low specific gravity, and contains a variable trace of albumen. In other cases we find signs of cystitis, the urine containing pus and mucus, and speedily undergoing ammoniacal decomposition, with a deposit of triple phosphate.

Theory of Gout.

That gout is a constitutional disorder cannot be doubted, when we reflect on its mode of development and symptoms, more especially on the multiplicity of its local manifestation. It is quite certain that when the characteristic features of the disease—the gouty deposits—are already present, there exists a morbid condition of the blood and humors—a *dyscrasia*. This was known even to the ancients; but to their knowledge modern research has added the information that the deposits consist chiefly of urates, and that, in fully-developed gout, the blood and humors are loaded with the same compounds, whence the progressive increase of the deposits. On these few data a variety of theories have been built—some designed to explain the dyscrasia, the "uric acid diathesis;" others, the occurrence of the periodic attacks of gout.

First, then, as regards the origin of the dyscrasia. Among the older theories, most of which are incompatible with our present knowledge, one only—that of Todd—deserves our notice. Todd put great stress on the digestive disorders by which the actual outbreak of gout is preceded. The morbid activity of the stomach and duodenum was thought by him to lead to the formation of lactic and uric acids, these acids entering into combination with certain elements of the bile retained in the blood, owing to simultaneous disorder of the liver. The gouty diathesis would thus depend on the blood being overloaded, not merely with uric acid, but with other excretory products also; nay, Todd went so far as to assert that gout might exist without the presence of uric acid in the blood at all. The latter assertion is wholly arbitrary, for, in the present state of science, the only characteristic feature of gout is the deposition of urates, and this must be due either to the presence of an excess of uric acid in the blood, or, supposing the proportion of uric acid to remain normal (and we know that this is exceedingly minute), on its being abnormally insoluble. That—apart from the accumulation of uric acid in the blood—there may be other changes in the composition of that fluid and of the humors generally is very possible—nay, not at all improbable; but we know nothing about such changes at present, and they can never acquire significance in our eyes so long as their connection with the pathognomonic deposits of urates has not been determined. Moreover, of all the substances which can accumulate in the blood to excess, uric acid and its salts are the least soluble, and therefore the most likely to be deposited.[1]

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[1] That a similar part to that of uric acid may be played by other compounds of sparing solubility has been shown by *Virchow's* discovery (see his Archiv, XXXV., 358, and XXXVI., 147) of deposits of guanin—a sort of guanin-gout—in pigs.

Todd's theory is chiefly based on the observed fact that digestive disturbances, such as gastric catarrh with formation of acid, are commonly attended by a sediment of urates in the urine. The occurrence of this sediment used formerly, and even now, to be frequently taken as proof of an increased formation and elimination of uric acid. The inference is quite wrong. There is not the slightest evidence of any real increase in the amount of uric acid produced in the system ; and even if there were, the increase could only be transient and of short duration, since the digestive disorder would tend to limit the supply of nourishment —of the material from which the uric acid is formed—and would thus interfere with any continued accumulation of the acid in the system—with the production of a uric acid dyscrasia. On the other hand, we are obliged to admit that disorder of the digestive functions, when the dyscrasia already exists, is an important element in the production of the gouty paroxysm, as we shall see more clearly farther on.

The more modern view, according to which the source of the augmented production of uric acid is to be sought in the amount and nature of the food—in the abuse of albuminous and fatty articles of diet—rests on a more secure foundation. It is commonly imagined that, owing to a luxurious habit of life and want of exercise, the nutrient matters taken into the system are imperfectly oxidized ; the alcohol and fatty matter, more especially, diverting the inspired oxygen from the albuminous compounds, which accordingly, instead of being converted into urea, remain at a lower point of oxidation as uric acid. Put in this way, however, the hypothesis is untenable, for the system is never deprived of oxygen, save in asphyxia ; moreover, it has been proved by Woehler and Frerichs that the formation of uric acid is not entirely due to a diminished power of oxidation. They found that when uric acid was artificially introduced into the body, whether of man or of the lower animals, it underwent conversion into urea, notwithstanding the fact that both in man and in animals a certain quantity of uric acid is constantly being eliminated as such. Did the latter merely represent a residue of imperfectly oxidized albumen, it would be difficult to explain its constant occurrence, seeing that an artificially added excess of this residual compound meets with no difficulty in becoming fully oxidized.

The origin of uric acid must therefore be referred to other causes, of which we are only able to point out a few, and this with only a certain degree of likelihood. There is much reason to believe that the spleen is, if not the only, yet a very important source of uric acid. When the spleen is enlarged, uric acid is produced in larger quantity than usual. We see this in splenic leukæmia, and in other instances brought forward by H. Ranke.[1] The spleen as a whole, and especially its constituent follicles, are liable to enlargement of a physiological kind also, viz., some hours after food, at a time when the products of gastro-intestinal digestion are being absorbed (Gray, Schoenfeld, Ecker). We find a corresponding increase in the amount of uric acid eliminated several hours after a meal. An abundant meal thus operates in a twofold manner to increase the production of uric acid: on the one hand, by furnishing the system with more materials for its formation (this is especially true of food rich in albuminoids); on the other, by exerting a specific influence on the functional activity of the spleen. Here we have a possible cause to account for the increased formation of uric acid in gluttonous persons, a cause which may possibly continue to operate for some time after their diet is reduced, for the repeated and considerable enlargement of the spleen may gradually have developed a chronic congestion and functional over-activity of that organ.

Whatever be the source of the uric acid, and whatever its significance, one thing is quite certain: that a diet rich in albuminoids (C. G. Lehmann,[2] H. Ranke), and especially in fatty matter (G. Meissner and Koch[3]), contributes greatly to increase the formation of uric acid. The same result follows the introduction of certain constituents of articles of diet which are more common at the table of the wealthy and luxurious than at that of the poor, viz., asparagin and malate of lime (Meissner, Koch). We are therefore quite justified in regarding that dietary which the common experience of physicians indicates as an important element in the causation of gout, as one of the principal causes of an increased formation of uric acid. But this is not enough to explain the characteristic deposits which occur in gout; for if the excess of uric acid be eliminated from the system as fast as it is formed, no accumulation can take place in the blood; and even if the rate of elimination fall short of that of production, there is no reason why larger quantities of uric acid than the normal minimum should not accumulate in the blood without being deposited anywhere, since that fluid is able to hold a much larger amount of the acid in solution than it is usually called upon to do. As I have already stated, an abnormal quantity of uric acid is produced in the system under various conditions (*e. g.*, in splenic leukæmia); this is partly got rid of by an increase in the amount excreted in the urine, while another part also, in excess of the normal average, is retained in solution by the blood and humors. The blood and humors will also contain an excess of uric acid when, the rate of formation being constant, elimination is interfered with, as in many forms of renal disturbance (nephritis, extirpation of the kidneys, ligature of the ureters); and yet neither under these conditions, nor in leukæmia, do we find deposits of urate of soda. It is only in birds and snakes, which normally produce a far greater amount of uric acid than man and other mammals, that arrested elimination is followed by an accumulation so great as to exceed the solvent capacity of the humors and to produce deposits which, as Zalesky[1] has shown, are quite analogous to those produced in gout.

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[1] Beobachtungen und Versuche über die Ausscheidung der Harnsäure. München, 1858.

[2] Zoochemie, p. 421.

[3] Nachrichten von der Königl. Ges. d. Wissensch. zu Göttingen. 1865. P. 182. Ztschrift. für rat. Med. XXIV., 267.

We are thus forced to conclude that in gout there is either so great a disproportion between the rate at which uric acid is formed and that at which it is eliminated as to cause it to accumulate in the blood to an extent beyond the solvent capacity of that fluid, or else that the solvent power of the blood itself is, for some reason or other, diminished.

It is upon the first of these alternatives that Garrod lays most stress. In his view of the matter, which is very generally accepted, the function of the kidneys is interfered with at a very early period in gout, and an accumulation of uric acid in the blood thereby promoted. The exciting causes of the actual paroxysm operate by sudden additional interference with the renal function, or by lessening the alkalinity of the blood, thus determining the precipitation of urates with the usual phenomena of acute gout. To this theory there is only one objection. It is true that the kidneys usually become affected during the course of the disease, especially in its irregular, chronic stage; but they are seldom found to be diseased at the time of the first attack of gout, or during the earlier "typical" stage. At any rate, during this early period we hardly ever find any symptoms of renal disease, such, *e. g.*, as albuminuria; moreover, the very rare occasions that have presented themselves of examining the kidneys after death in this initial stage of gout have not hitherto furnished evidence of any serious morbid change in them. It has also been suggested that the kidneys may be irritated and brought into an inflammatory condition by the excess of uric acid formed and eliminated before the actual outbreak of gout. But this view is quite opposed to our experience of leukæmia; leukæmic patients go on for years excreting abnormally large quantities of uric acid without getting any sort of renal inflammation.

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[1] Untersuchungen über den urämischen Prozess und die Funktion der Nieren. Tübingen, 1865.

These more than doubtful speculations concerning the existence of renal mischief at the very outset of gout are quite unnecessary for the explanation of many—or rather of most—cases of the acquired disease. Conditions similar to those which cause a premature deposit of uric acid and its salts in urine, without their quantity being really augmented, may also occur in the interior of the body; they will then give rise to the precipitation of a quantity of uric acid which might, under ordinary circumstances, have remained dissolved in the blood and humors.[1] Among these conditions is *an increase in the proportion of acids or of acid salts.*

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[1] A case of extensive gouty concretions occurring in a pigeon, whose uropoëtic organs were perfectly healthy, has been recorded by *Siedamgrotzki* (*Virchow* und

Now, it is a striking fact that the chief causes of gout (putting aside hereditary predisposition), viz., over-indulgence in albuminous food, and disturbances of digestion, both tend to augment the production of acid in the system. Food rich in albuminoids, besides furnishing materials for the formation of uric acid, serves as a medium for the introduction of acid salts (phosphates) or even of free acids into the system; further, it gives rise to the formation of phosphoric and sulphuric acids in such excess as actually, in many instances, to increase the acidity of the urine. Again, as regards disturbances of digestion, we know that they contribute to generate organic acids (lactic acid, volatile fatty acids) in abundance; and it is clear that these acids, becoming absorbed, may diminish the alkalinity of the blood.

Accordingly we see that in gout a whole series of circumstances combine to increase the formation of uric acid, and at the same time to lessen the solvent capacity of the humors. Trifling causes may then suffice to cause precipitation of uric acid or its salts, and to bring on a paroxysm of gout. For we may regard it as certain that the acute paroxysm is due to the irritation set up by the urates in the tissues amid which they are deposited.

Whether the precipitation of the urates shall occur in the kidneys and urine, or at an earlier stage—from the tissue juices—depends on circumstances of whose nature we are absolutely ignorant. In the former event, we get lithiasis, a formation of gravel and calculi; in the latter, gout. This is the obvious relation between the two disorders; they often occur together in the same patient; the difference between them referring solely to the locality where the precipitation of urates takes place.

How comes it that in gout the urates are deposited, in the first instance, in cartilage—a tissue containing no proper blood-vessels—and in those joints which are farthest from the heart? This may be explained by supposing that some part, at least, of

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Hirsch, Jahresbericht, 1873. II. 617); it illustrates the importance of this question of insolubility, and proves that the latter is sufficient of itself to cause a precipitation of urates, without help from disease of the urinary apparatus.

the uric acid may be formed in the tissues themselves, and carried away by the lymph; possibly, too, the urates may be even less soluble in the lymph than in the blood itself. It has been shown by Zalesky and Chrzonszewsky[1] that the uric acid deposits, produced artificially by arresting renal elimination, occur first and most abundantly in the juice-canals and lymphatics. Further, we must reflect that in the more distant parts of the body the venous circulation is sluggish, thereby facilitating passive congestion and transudation. Lastly, as regards the special liability of the metatarso-phalangeal joint, we must take into account a fact insisted on by Hueter, viz., that this very joint is commonly affected by simple panarthritis in oldish persons, and the previous existence of this inflammatory mischief tends to localize the effects of the uric acid diathesis.

The connection between chronic lead-poisoning and gout, which has only been recognized of late years, depends, in all likelihood, on a variety of convergent conditions. In the first place, the urine, under the influence of lead, grows scanty and highly concentrated, thus promoting an accumulation of uric acid in the system; then, again, the digestive functions are usually disturbed by lead, even without actual colic; further, it may be that lead impairs the solvent power of the blood directly; finally, lead-poisoning is among the causes of nephritis (Ollier, Lancereaux, Tardieu, Biermer, etc.), to which the simultaneous abuse of intoxicating liquors may likewise contribute.

The nephritis which gradually sets in during chronic gout, and leads to contraction of the kidneys, must obviously contribute to keep up the accumulation of uric acid in the blood; and the results of experiment show conclusively that when this accumulation becomes very great, the uric acid may be deposited in the internal viscera as well as in the joints; chalk-stones may form in them, as shown by the post-mortem results already alluded to, few as they still are. Here, as in the joints, the precipitation of uric acid is greatly favored by a sluggish circulation; and this is possibly the reason why persons with a tendency to venous congestion—*e. g.*, of the hemorrhoidal veins —and those in reduced health, are especially prone to suffer from those internal maladies which we should be fully justified in calling "visceral gout," had we only some criterion whereby to distinguish them from similar affections due to other causes. (*Vide* p. 114.)

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[1] *Virchow's* Archiv, XXXV. 174. See also *Pawlinoff*, ibidem, LXII. p. 57.

Again, it is not impossible to suggest an explanation of the way in which the joint-affection and the internal disorders alternate with one another. (Masked, metastatic, and retrocedent gout.) We may fairly imagine that blood impregnated with uric acid, and possibly with other abnormal constituents also, may cause various troubles which refuse to subside until a certain excess of the impurities in question has been got rid of by precipitation in the joints; and conversely, that when the joint-affection is suddenly arrested in the full course of its development by any cause (*e. g.*, exposure to severe cold), an internal disease, a form of "retrocedent gout," may be brought on. In the majority of cases, however, in which internal disease coincides with a relatively mild form of arthritis, the former may be attributed to the enfeeblement of the patient's constitution by previous attacks; for when many such attacks have occurred, the tissues about the joints become more or less completely saturated, the vessels obliterated and impervious, so that a further exudation and precipitation of urates in the same vascular area may become less and less possible, and finally, altogether impossible. Then it is that the typical joint-affection ceases to occur; in its stead we find mere suggestions of a paroxysm, which, in the teleological language of the older physicians, were termed "fruitless attempts at a crisis."

Diagnosis.

Regular gout can hardly be taken for anything but what it is; for the sudden onset of the joint-affection with acute pain in the middle of the night, after previous disorder of digestion, is a characteristic phenomenon, which has no parallel in the history of any other local or constitutional malady. Traumatic inflammation of the great toe-joint might, indeed, exhibit the same appearances; but even then the previous history and condition of the patient, the absence of the predisposing causes of gout, the signs of injury, would easily insure a correct diagnosis. Still less likely are we to mistake gout for rheumarthritis (see chapter on diagnosis of the latter).

Chronic or irregular gout, when several joints are permanently swollen, may be mistaken for *arthritis deformans*, especially for that form in which the joints of the fingers and toes are involved. The two diseases may be distinguished from each other by considering the antecedent circumstances of the patient—arthritis deformans being a disease of the poor, of the female rather than of the male sex, while the converse is true of gout. Again, the patient's habits, and a history of previous attacks of regular gout, may throw light upon the case, for arthritis deformans is gradual in its development; it usually progresses symmetrically on both sides of the body (in this respect unlike gout), and it is not associated with those alterations in the urine which are so common in gout. Finally, in a doubtful case, the discovery of chalk-stones elsewhere (*e. g.*, in the auricle) or of urate of soda in the blood by Garrod's thread-test, would decide us in favor of gout.

As regards internal or visceral gout, the circumstances which might lead us to infer its existence in any case have already been discussed (p.114).

Course, Duration, and Issues.

From the descriptions given above, the reader will have already learned that gout runs a very tedious course, extending over a series of years. In its regular form the paroxysms are separated from one another by intervals of various length, during which the diathesis continues latent, *i. e.*, gives rise to no symptoms, or to symptoms which are trifling and by no means distinctive. When circumstances are favorable, and the malady does not pass into its chronic form, it usually persists till life is brought to a close by other causes. Complete recovery from gout is among the rarest of exceptions, while, on the other hand, death scarcely ever results directly from the regular form of the disease.

Chronic gout usually ends in death after a variable number of years. The fatal issue is immediately due to organic mischief brought on by the combined operation of the gouty diathesis, the complications which so frequently attend it, and the advanced age of the patient. The organic mischief commonly belongs to the category of senile degenerations, and gives rise either to a lingering cachexia, to which the patient succumbs gradually, or to sudden death, with the symptoms of apoplexy or angina pectoris.

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Prognosis.

This is unfavorable as regards complete and permanent recovery. Any real arrest of the morbid process usually demands as an indispensable preliminary a complete revolution in the patient's mode of life, and to such a revolution surrounding circumstances and the inclinations of the patient himself usually form an insurmountable hindrance. Patients who have enough self-control to give up their old habits, and to adopt and carry out a suitable rule of life, may keep their gout down for a long term of years, shorten their sufferings most materially, and reach a comparatively vigorous and tranquil old age. An opposite line of conduct carries its punishment with it.

The more irregular the type of the disease, the more it is complicated by visceral disorders and a general impairment of nutrition, the less chance there is of even temporary improvement—of intervals of perfect freedom from suffering,—and the greater is the danger to life.

The prognosis of hereditary gout is usually less hopeful than that of the acquired disease, the former being more obstinate and more prone to pass into the irregular variety.

As regards the individual paroxysm, the following indications may be viewed as favorable: the limitation of the disease to few joints, or, better still, to one joint only, especially if that joint be a toe; acute fever; severe local inflammation, with great pain; strict periodicity of occurrence. The more marked all these features are, the better is the prospect of a period of unbroken health to follow the attack, and the longer may this period be expected to last.

Treatment.

The treatment of gout may be considered under three heads: 1st. Treatment of the gouty diathesis; 2d. Treatment of the paroxysm; 3d. Treatment of the morbid changes induced by gout in internal and external organs—of the local products of diseased action.

The treatment of the gouty diathesis consists in the adoption of measures similar to those enjoined, by way of prophylaxis, on persons hereditarily predisposed to the disease, or on those who have become, in consequence of their own self-indulgence, appropriate subjects for its development, and who are already suffering from the disorders that herald its approach—the so-called "premonitory symptoms." Those who have much to do with lead and its preparations ought, moreover, to guard themselves against the injurious effects of this metal by adopting the various precautions primarily designed to ward off lead-poisoning, but tending likewise to prevent gout.

1. *Treatment of the Gouty Diathesis.*

Foremost among the measures pertaining to this branch of our subject stands the due regulation of diet and mode of life. Without this, all the vaunted remedies and plans of treatment—and they are legion—will fail, while, on the other hand, this alone will often prove to be an adequate substitute for all medicinal agents of whatever kind.

What I have already said about the influence of diet, in discussing the etiology and pathology of gout, is enough to show that albuminous and especially fatty matters should be very sparingly indulged in, and never allowed to burden the digestive apparatus either by their quantity or otherwise; further, that all food likely to irritate the kidneys should be strenuously avoided. Roughly speaking, the diet should be vegetable rather than animal. Spices and other stimulating condiments should, as far as possible, be excluded in preparing the food. Abstinence from meat must not, of course, be pushed so far as strict vegetarianism, for in the majority of cases, at any rate, it would be impossible to enforce a vegetarian regimen for any length of time; it is difficult enough to induce the patient to substitute a simple and non-stimulating dietary for those pleasures of the table to which he has been used. Extreme measures in this respect are not only impracticable, but undesirable, for the patient, if restricted to vegetables, would be obliged to consume them in inordinate quantities, and to overload his stomach, in order to retain some degree of bodily vigor. It must always be remembered that the object of treatment is not to weaken the patient, not to lower the general level of his nutrition, but merely to modify what is abnormal in his diet. An eliminatory course of treatment, pushed to extremes, or a very sudden change in the patient's habits, is often badly borne; collapse may ensue, or the constitution may be undermined, thereby facilitating the transition from regular to atonic gout, whose future prospects we have already shown to be so far from hopeful.

A mixed diet is accordingly the best—a diet containing a minimum of fatty matter, and in which the proportion of albuminoids, especially of meat, is regulated in each individual case with due regard to constitutional strength, digestive power, occupation, etc. As a general rule, gouty persons should only eat meat once a day, at their chief meal. Smoked and salt meat and fish, pork, cheese, farinaceous compounds containing much oily matter and highly spiced,—indeed, all culinary delicacies—should be absolutely forbidden. Eggs and dishes containing them should be avoided as much as possible; the yolk must be considered particularly noxious, owing to the quantity of oily matter and lecithin (an abundant source of phosphoric acid) it contains. On the other hand, all kinds of soup, the more delicate varieties of meat, fish, shell-fish (oysters) in moderation, fresh vegetables, and fruit, may be recommended.

Tea and coffee should be altogether abjured, or, when the patient cannot bring himself to do this, should be taken very weak; milk, acorn-coffee, or an infusion of roasted cocoa-nibs, may be substituted. The patient's drink at meal-times should be water—either plain water or one of the natural or artificial carbonated waters containing alkalies or alkaline chlorides (soda-water, Seltzer, Faching, Bilin, Giesshuebler Sauerbrunnen, carbonate of lithia, etc.). Alcoholic liquors should never be taken to quench thirst, but only as roborants, when they are really needed; the best form is then a good red wine, neat or diluted with water, or else a light beer brewed with a small proportion of hops; the fiery southern wines, and those which are acidulous, champagne, and heavy beer (porter, etc.), must be forbidden.

To prevent overloading of the stomach, the number of meals should be limited. The principal meal, or dinner, should not be put off to a late hour; no food but what is strictly needed to allay the cravings of hunger should be taken in the evening. I need hardly say that no universal dietary can be framed to suit all cases. Even in any individual case, alterations must be made from time to time, according to the stage of the disease and the condition of the patient's strength; a spare diet may be indicated at one period, a nourishing one at another. Further, the physician must attend to certain idiosyncrasies and to the personal experience of the patient; the latter is often the best judge of what articles of diet are likely to injure him and bring on an attack of gout.

Active exercise is of great importance. Its usefulness in gout depends, not, as was formerly supposed, on its causing a more active metamorphosis of the nitrogenous matters and a quicker oxidation of uric acid—for in this respect exercise can do little or nothing[1]—but because it uses up those oily compounds whose accumulation in the system has already been shown to promote the formation of uric acid. Appropriate exercise, moreover, stimulates digestion and quickens the circulation of blood in the veins, partly by the mechanical influence of muscular contraction on these vessels, partly by quickening the respiratory movements and thereby aiding the aspiration of blood from the systemic veins; it likewise increases the elimination of carbonic acid, whose accumulation in the blood causes arterial contraction by stimulating the vaso-motor centres, and thereby gives rise to venous congestion. For all these reasons, exercise is especially beneficial to corpulent people who suffer from constipation and hemorrhoids; it ought likewise to be enjoined on other gouty subjects as well, in due proportion to their strength. When active exertion (walking, riding, gardening, hunting, gymnastics, etc.) is forbidden by stiffness of the joints, carriage exercise, friction and shampooing of the limbs, must take its place. These measures may be judiciously supplemented, in recent cases, before the development of constitutional cachexia or of internal disease, by rubbing the body with cold water or brine. Cold bathing has been proved by experience to be unadvisable; it may easily bring on an attack of gout, or set up organic disease. Sea-bathing ought only to be resorted to by young and vigorous subjects, and then only under great precautions.

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[1] The data we possess concerning the effects of exercise on the quantity of uric acid eliminated are very contradictory. *Hammond* and *Boecker* state that it is diminished; *Genth* and *Heller*, that it is increased; while *H. Ranke* found the uric acid diminished by gentle exercise, increased by fatigue. Finally, *Bence Jones* was unable to make out any constant relation between bodily exercise and the elimination of uric acid.

Gouty persons should be warmly clad, wearing flannel next to the skin, and should live in dry houses. Those whose circumstances allow them to migrate to a warmer climate at the approach of winter often find the change effectual in warding off an attack.

Finally, the patient must be advised to exercise the utmost self-restraint in sexual indulgence; late hours, excitement, severe study, etc., ought also to be forbidden.

The treatment of the gouty diathesis by milk, whey, fruit, or water, belongs in some measure to the present division of our subject. Every one of these methods has had its enthusiastic advocates, especially in days gone by. The principal share of the credit which they undoubtedly deserve when employed in suitable cases may safely be ascribed to the rigorous and systematic carrying out of an appropriate regimen—a feature common to all of them. The regular addition of a fixed quantity of milk, whey, fruit, or water to this common element merely stamps it as a "special" course of treatment or "cure." But not every stomach can put up with such remedial methods ; and before we come to a decision, it is usually advisable to make a preliminary trial in order to find out which of the substances above enumerated, and in what quantities, is best tolerated by the system. The hot-water cure of Cadet de Vaux—formerly vaunted as an unfailing remedy both for the gouty diathesis and the paroxysm —is still less suited for general adoption. It consists in taking a plate of soup at bed-time, and, on the following day, swallowing from six to eight ounces of water as hot as can be borne every fifteen minutes for twelve hours ; the treatment is then concluded with another basin of soup. Should this not have cured the patient, he is directed to repeat the process after an interval. A method such as this few patients are able to bear ; many have succeeded in ruining their digestion by its means, and it has even been known to be followed by sudden death.

Treatment by mineral waters is at once more suitable and more effective. Certain alkaline, alkaline-saline, and alkaline-muriatic waters enjoy a well-merited reputation in the treatment of gout. Here, too, the way the patients' habits are regulated has a good deal to do with the beneficial effects ; people submit to irksome restraint more willingly when they are taking the waters than at other times. Again, a pure air and plenty of exercise, with the other adjuncts of life at a watering-place, contribute their share to the sum total. The water itself, independently of the salts dissolved in it, does good ; when taken habitually in considerable quantities it stimulates the secreting organs, especially the kidneys and bowels ; it likewise increases the solvent power of the blood and humors by diluting them. It is just possible that taking large draughts of plain water may exert some influence on the formation of uric acid, for Genth asserts[1] that the proportion of uric acid in the urine is thereby diminished. But, after all these influences have been fully allowed for, we find it impossible to deny that the special ingredients of the different waters, viz., the carbonate and bicarbonate of soda, chloride of sodium, the alkaline and earthy sulphates, possess distinct remedial virtues. They principally tend to remove the various disorders which stand in a more or less close degree of causal relationship to gout, either as antecedents or concomitants. I allude to the irregularities of digestion, the gastric and intestinal catarrh, the tendency to acidity, the constipation and portal congestion, the disorders in the urinary secretion, etc. But the salts in question, more especially the alkalies, carbonate of soda, carbonate of lithia (so largely recommended of late years), and chloride of sodium, are also believed to exert a more immediate influence upon the gouty diathesis and the uric acid dyscrasia, this belief resting on the observed fact that the sediment of urates frequently disappears from the urine under their administration. But this result is partly due to the altered reaction of the urine (effect of alkalies), partly to its being less concentrated (diuretic action of the various salts). And even supposing that the absolute amount of uric acid eliminated were diminished during the administration of the above salts (a fact which is far from certain[1]), the effect would only be temporary and palliative, lasting while the waters were continued only, and capable of being achieved by large draughts of plain water likewise (Genth—*vide infra*). Our chief object must always be—so long as no profounder changes have occurred in internal organs—to get rid of the disturbances of digestion and circulation; the nature of those disturbances, as well as of any complications that may be present, must guide us in our choice of a watering-place, the patient's strength and the stage of his malady not being left out of account. For the rest, there is hardly any watering-place of repute in the treatment of gout which does not fulfil several of these indications at once by the variety of remedial measures it supplies, the variety of salts contained in its different springs, the graduation of temperature, the simultaneous employment of general or local baths, etc.

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[1] Untersuchungen über den Einfluss des Wassers auf den Stoffwechsel. Wiesbaden, 1856.

When gastric catarrh with acidity forms the leading symptom, while the patient's strength is otherwise good, and he only suffers from occasional attacks of regular gout, with perhaps a tendency to gravel, Vichy water or the weaker alkaline water of Neuenahr is peculiarly appropriate; if mucus is largely secreted, Ems water may be preferred. When portal congestion coexists with great obesity, and there is not much digestive disturbance, Marienbad (Kreuzbrunnen) is indicated; or, when the liver is actually enlarged, and there is more or less jaundice, Karlsbad—the particular spring to be selected which is most appropriate to the patient's excitability, passing from the colder to the hotter ones. Karlsbad water is always very serviceable when the urinary secretion is out of order, and there is much sediment thrown down. In weaker subjects, or in those whose constitution has been to some extent enfeebled by protracted gout, the waters of Kissingen or Homburg, or, when the hemorrhoidal tendency is very pronounced, those of Franzensbad should be preferred to the sulphate of soda springs just mentioned. Drinking the Wiesbaden waters and bathing in them is often of great value, especially in old cases of gout which are passing into the chronic form. A course of Wiesbaden waters not unfrequently brings back the typical paroxysms with long intervals of relative health. The effects of the Baden-Baden waters are similar in kind, but milder in degree.

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[1] *Muench* (Archiv des Vereins für gemeinschaftliche Arbeiten VI. 398) found the uric acid diminished in amount; *Severin* (Ueber die Einwirkung des kohlensauren Natrons, etc. Dissert. Marburg, 1868) was unable to confirm his statements.

Very decrepit persons, for whom we dare not prescribe the drastic purgative waters which exert a profound alterative influence on nutrition, are greatly benefited by ordinary warm baths —the akratotherma—(Gastein, Wildbad, Pfaeffers, Plombières, Bath, and Buxton).

We know of no strictly medicinal agent that is capable of curing gout. Many such agents have been sought for and recommended in the course of centuries, some on purely empirical, others on theoretical grounds.

Among empirical remedies, colchicum has enjoyed the reputation of an anti-arthritic for a longer period than any of its rivals, and to this day it finds many advocates. The majority of physicians, however, even in England, where the drug is still most popular, have gradually abandoned its use in the gouty dyscrasia, in which its efficacy is more than doubtful, while its continued administration unquestionably tends to upset digestion, to irritate the kidneys, and to shatter the nervous system of the patient. Hence its use is all but entirely restricted nowadays to the treatment of the paroxysm.

Alkalies have long been recommended and largely used on theoretical grounds, in order to combat the uric acid dyscrasia. The carbonates and compounds of potash and soda with the vegetable acids, lime water and magnesia, and above all the recently introduced carbonate of lithia, are certainly able to hinder the deposition of uric acid in the body—whether by increasing the solvent capacity of the blood or by forming soluble urates. In this way they help to delay the gouty paroxysm. But their power is necessarily limited; for, as they cannot in any degree prevent the formation of uric acid, they are unable of themselves to cure gout. But they are very useful as auxiliary measures when associated with such measures as diet and mineral-water cures, which modify the entire course of the nutritive processes. They may also contribute to the removal of the morbid products—the gouty deposits—a subject to which we shall have to return farther on.

Other remedies, whose temporary popularity was based on chemical theories, some of which were wholly erroneous, *e. g.*, carbonic acid (Parkin), benzoic acid and benzoate of soda (Ure, Briau), silicate of potash (Ure), have fallen into just oblivion.

Better results may perhaps be anticipated from sarkosin, a substance which has not yet made its way into any pharmacopœia. Schultzen[1] asserts that if a sufficient quantity of it be taken, uric acid and urea disappear entirely from the urine; and that, more particularly in fowls, we find the uric acid replaced by freely soluble compounds of sarkosin with other radicals. Supposing these statements to be correct, we have at our disposal a means of checking the *formation* of uric acid, thereby effecting even more completely the object we have in view when we alter the patient's diet. Unfortunately, the difficulty of preparing sarkosin, and its high price, must for the present interfere with its clinical trial in cases of gout.

Finally, some allusion must be made to the vegetable bitters

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[1] Berichte der deutschen chemischen Gesellschaft, 1872, p. 578.

(trifolium, gentian, calamus, quassia, cinchona, Portland powder) either alone or in combination with tonics; of course they cannot lay claim to any specific anti-arthritic virtues, but they may serve, especially in the latter stages of the disease, to restore the digestion and strength of the patient.

2. *Treatment of the Paroxysm.*

The main principle by which we must be guided in this part of our subject is—to abstain as far as possible from active interference so long as the attacks maintain their typical character. For we do not often succeed in cutting short a paroxysm; and if we do, our success may be immediately followed by disagreeable consequences. Violent measures, such as the application of cold, bloodletting, and drastic purgatives, may easily disturb the normal course of the attack, and delay the progress of convalescence.

As soon as the premonitory symptoms of a paroxysm make their appearance, the patient should be confined to bed, strictly dieted, and directed to quench his thirst with plain water, or with one of the carbonated waters mentioned above. Should his bowels be confined, the mildest measures only must be resorted to (clysters); active purgation must be avoided; troublesome nausea and pyrosis must be relieved by effervescing draughts, carbonate of soda, carbonate of magnesia or simple magnesia. An emetic should be reserved for exceptional cases, when some gross error of diet has been committed, and the stomach is much embarrassed; when a tendency to vomit already exists, it may be most safely promoted by draughts of lukewarm water.

During the actual paroxysm, the affected limb should be kept raised; the joint, when the inflammatory symptoms are at all severe, should be kept warm, without, however, allowing it to become overheated; it may be wrapped in a single fold of cotton-wool or flannel. Local bloodletting should never be resorted to except as a last resource, when the inflammatory swelling is severe; when the pain is unbearable, it may generally be relieved by narcotic ointments and hot fomentations; or a subcutaneous injection of morphia may be given, or an opiate internally. Chloral, according to O. Liebreich,[1] should only be given to gouty patients simultaneously with alkalies (carbonate of soda or of lithia), lest the formic acid generated by its decomposition in the system do positive harm in connection with the existing uric acid dyscrasia.

Of other internal remedies, colchicum alone deserves a trial. That it is useful in shortening the paroxysm cannot be denied; its power in this respect is affirmed by the most experienced physicians, especially in England, though we do not know how it is exercised. But it should only be given to patients who retain their bodily vigor, and not in the atonic form of gout; moreover, we ought not to prescribe the large doses which used formerly to be popular, and which cause nausea, vomiting, and severe diarrhœa. The operation must be closely watched. Many physicians, *e. g.*, Gairdner and Charcot, recommend the administration of colchicum, not at the outset of the paroxysm, but when it culminates. The best way is to begin with moderate doses, and to increase them gradually as the paroxysm approaches its end (twelve to twenty drops of the tincture or wine of colchicum seed three or four times a day, gradually raising the dose to thirty drops). The remedy should be discontinued as soon as nausea, slowness of the pulse, or giddiness set in; a copious flow of urine and abundant perspiration are signs that it is acting favorably. If there be severe diarrhœa, the colchicum may be combined with tincture of opium; many authors ascribe the good results chiefly to the latter drug. When the bowels are confined, the colchicum may with advantage be combined with gentle aperients, *e. g.*, a saturated solution of carbonate of magnesia in vinegar of colchicum (carbonate of magnesia, fifteen grains; sulphate of magnesia, from two to five scruples; peppermint water, one fluidounce; vinegar of colchicum, from forty-five to eighty minims; syrup of saffron, forty-five minims. After Scudamore).

Should the inflammatory symptoms not be well marked, we ought to try (so the old school used to teach) and convert the

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[1] Das Chloralhydrat. III. Auflage. Berlin, 1871, p. 80.

"torpid" type of local action into an "acute" or "sthenic" one; we ought, as far as possible, to promote the elimination (the "crisis"), so as to hinder any metastasis of the disease to internal parts. I have already explained the relation between these principles of treatment and our modern views. I have pointed out that, owing to repeated inflammation of the joint and periarticular tissues, and their infiltration with urates, augmented during each successive attack, the local circulation may be interfered with and the vessels more or less obliterated, so that no fresh deposit—at all events, of any magnitude—can take place in the area supplied by them. Still, by the application of powerful irritants, we may excite a certain degree of hyperæmia in the skin and surrounding parts; and even when this leads to nothing and fails to bring on a regular attack of gout, some derivative effect is nevertheless achieved, which may prove at least as beneficial as that produced by counter-irritation generally, when a tendency to congestion of internal organs or to nervous accidents exists. And as certain parts—viz. the joints formerly affected—are already predisposed to congestion, it seems quite reasonable to select them for the application of our derivative remedies, whether we believe in the "critical" nature of the joint-affection or not. In those cases, at any rate, where the joint-affection is sluggish in its development and there is some threatening of inward mischief, or where wandering pains in the limbs coexist with great restlessness, we shall do well to excite as active a congestion as we can about the joints, in order to "localize the disease" or to "attract the morbid process to the joints." The urgency of the symptoms, the special circumstances of the case, the fancies of patient or physician, must determine the choice of the particular measure to be adopted. Of course the milder ones should always be tried in the first instance, *e. g.*, wrapping the joints in hot flannel, hot sand-bags, fumigations, stimulating local baths, friction with alcoholic irritants; we may then gradually proceed to employ more vigorous measures, such as mustard poultices, ammoniacal liniments, blisters, or even moxas.

Counter-irritation applied to the joints does not of course exclude the use of other derivative measures, whose nature and point of application must be governed by the organ affected (head, thoracic viscera). Among these measures are dry cupping, or even, in special cases, local abstraction of blood. Similarly, stimulant or analeptic remedies may be given internally, suiting the remedy to the particular requirements of the case (aromatic infusions, ether, camphor, musk, preparations of ammonia). Finally, the local affections which may become developed should be managed on general principles, and with continual reference to the state of the patient's strength.

When the attack is over the affected joint may with advantage be subjected, first to passive, then to active movement. Oily preparations may be rubbed in with a view to promote the absorption of exuded matters, and to prevent the articulation from becoming stiff.

LEEDS & WEST-RIDING MEDICO-CHIRURGICAL SOCIETY

3. *Treatment of the Local Effects of Gout.*

Foremost among the local changes caused by gout are the deposits in and around the joints—the chalk-stones,—together with the inflammatory thickening of the tissues and the consequent articular stiffness, dislocations, contraction of tendons, etc. Our attempts to remedy these evils must partly be conducted in accordance with the methods already laid down when speaking of the treatment of the gouty diathesis, viz., mineral-water cures, exerting a powerful stimulant effect on the secretions. Their action in promoting absorption of the morbid products is appreciably seconded by the simultaneous use of baths, local and general; at most of the watering-places I have enumerated, the springs are employed for this purpose as well as for drinking. The "indifferent" waters (akratotherma) operate in a similar manner. But in addition to these we have a number of thermal waters principally employed for bathing purposes, which are to be preferred in those cases where the local deposits are considerable, and the functional disorders to which they give rise—the stiffness and pain—have become very prominent. Many of these thermal waters, though chiefly used for bathing, are also used, when sufficiently diluted, for drinking; or the patients, while going through a course of the baths, are made to drink at the same time one or other of the natural or artificial waters enumerated above, according to the special indications in each case. When the gouty diathesis, the complications, and the local deposits are all equally in need of attention, it is wise to begin with a course of one of the above-named waters internally, and to follow this up with baths at one of those bathing resorts which are specially efficacious in promoting absorption of the morbid products. The latter are, for the most part, identical with those in repute for the treatment of chronic rheumatic arthritis; of the alkaline thermal springs the most famous is Teplitz; of the sulphuretted ones, Aix-la-Chapelle and Burtscheid, Nenndorf, Baden near Vienna. The sulphuretted waters are chiefly indicated when the gouty malady happens to be complicated with affections of the skin, or when the chalk-stones have formed abscesses. They are also likely to be beneficial in cases of gout brought on by chronic lead-poisoning.

Among other internal remedies the alkalies are the most effectual in promoting solution of the uric acid deposits. They may be given in conjunction with mineral waters when the latter do not contain them in sufficient proportions, or they may take their place during the intervals of the mineral-water cure. The preparations of potash and soda, lime and magnesia, which used formerly to be prescribed, have recently been almost entirely displaced by lithia, ever since Lipowitz[1] discovered that the compound of lithia with uric acid is the most soluble of all its salts. From one-and-a-half to four-and-a-half grains of the carbonate of lithia, made into a powder with sugar, may be given several times a day. Ditterich[2] recommends four-and-a-half grains in five fluidounces of distilled water with a fluidrachm of liquorice juice, a tablespoonful to be taken every hour or every two hours. Finally, the lithia water prepared by Struve or Ewich may be taken as a beverage in sufficient amount to introduce from thirty to forty-five grains of the carbonate into the system daily (from two to three quarts of Struve's water).

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[1] Annal. der Chemie und Pharm. XXXVIII. p. 348.

[2] Blätter für Heilwissenschaft, 1870.

It may be that the chloride of lithium contained in several natural mineral waters (Baden-Baden, Salzschlirf, Duerkheim) is even better than the carbonate, the latter being converted into the former in the stomach.

Iodide of potassium has sometimes proved serviceable in promoting the absorption of chalk-stones, and especially the healing of gouty ulcers.

All internal remedies may be assisted in their operation—according to the exigencies of the particular case, the degree of pain and inflammation, etc.—by warm fomentations, inunctions, salves, or plasters. Remak[1] has found the transmission of powerful galvanic currents through the swollen joints to be beneficial. Passive movement of the affected joints is especially valuable, combined with manual friction—vaunted years ago by van Swieten, Grosvenor, and others; the parts may also be rubbed with dry, greasy, or medicated flannels, etc.

As regards the morbid products localized in internal organs, we must wait until their gouty nature has been proved, or at all events rendered probable (*vide* p. 114), before we take this into account in their treatment. The evidence is least imperfect in the case of the urinary organs, for here the state of the urine affords some information. They must be treated in connection with the diathesis as a whole; for the treatment of lithiasis is, in the main, identical with that of the gouty dyscrasia. Disease in other organs must be treated on general principles, saving that when we have reason to suspect that the organic malady is connected with that of the joints, we may find it desirable to apply derivative measures to the latter. This is a point which has already been discussed (p. 142).

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[1] Galvanotherapie. Berlin, 1858, p. 413.

ARTHRITIS DEFORMANS.

LITERATURE.—*Sydenham*, Observatt. med. Lectio VI. cap. 5, ed. Lugduni Bat. 1761, p. 272.—*Landré-Beauvais*, Doit-on admettre une nouvelle espèce de Goutte, etc. Thèse, Paris, 1810.—*Haygarth*, A clinical history of the nodosity of the joints. London, 1813.—*B. Brodie*, Pathological and surgical observations on diseases of the joints. London, 1818.—*Bell*, Remarks on interstitial resorption of the neck of the thigh-bone. Edinb., 1829.—*R. W. Smith*, (a) Dublin Journal of Med. Sciences, 1834, VI., Septbr. and 1843. (b) A treatise on fractures in the vicinity of joints. Dublin, 1847.—*R. Adams*, (a) In *Todd's* Cyclopedia of anat. and phys. Article: Hip-joint. London, 1839. (b) A treatise on rheumatic gout or chronic rheumatic arthritis of all the joints. London, 1857. (c) Med. Press and Circ., 1868, June, p. 516.—*Colles*, Dublin Journal, 1839, July.—*Knox*, Edinb. Med. and Surg. Transactions, III.—*Wernher*, Beiträge zur Kenntniss der Krankheiten des Hüftgelenks. Giessen, 1847, S. 39.—*Edward Canton*, London Med. Gaz., 1848, VI. and VII.—*Santesson*, Om höftleden. Vide Schmidt's Jahrb., Bd. LXXV., S. 266.—*Deville*, Bull. de la Société anatomique, 1848, XXIII., S. 142.—*Broca*, ibidem, 1850, XXV., S. 435, and Gaz. des hôp., 1851, No. 22.—*J. F. H. Albers*, Die marasmische Knochengicht. Deutsche Klinik, 1849, No. 25 u. 26; 1850, No. 27.—*Schoemann*, Malum coxæ senile, Jena, 1851.—*Zeis*, Beiträge zur path. anat. des Hüftgelenks. Nova act. acad., Leopold, 1851.—*Charcot*, (a) Etudes pour servir à l'histoire de l'affection décrite sous les noms de goutte asthénique primitive, etc. Paris, 1853. (b) Des déformations produites, etc. Mouvement Méd., 1873, No. 45.—*Trastour*, Du rhumatisme noueux. Thèse, Paris, 1853.—*Gurlt*, Beiträge zur pathol. Anatomie der Gelenkkrankheiten. Berlin, 1853, S. 182.—*Friedländer*, De malo coxæ senili. Diss. Breslau, 1855.—*Ritter*, Ueber die chronische deform. Gelenkentzündung. Diss. Göttingen, 1856.—*R. Hein* in Virchow's Archiv, XIII., S. 16.—*C. O. Weber*, ibidem, S. 74.—*Lasègue*, Arch. Gén. de Méd., 1856, Août.—*Roser*, Archiv f. physiol. Heilkunde, 1856, S. 369.—*Führer*, Handbuch der chir. anatomie, 1857, S. 275.—*Schuh*, Wiener Med. Ztschr., N. F. III., 1860.—*Henri Colombel*, Recherches sur l'arthrite sèche, Paris, 1862.—*R. Virchow*, (a) Die Krankhaften Geschwülste, 1863, T. S. 460. (b) Zur Geschichte der Arthritis deform. Sein Archiv, 1869, XLVII., S. 298.—*R. Volkmann* in v. Pitha u. Billroth's Handbuch der Chir., II., 1865, S. 555.—*v. Thaden*, Ueber spondylitis

deform. in Langenbeck's Archiv, IV., S. 565.—*Blezinger*, Spondylitis deform. Tübingen Diss., 1864.—*Guéneau de Mussy*, Du traitement du rhum. noueux, etc. Bull. de Thérap., 1864, Septbr.—*Trousseau*, Bull de Thérap., 1865, LXVIII., S. 58, et seq.—*Costa*, Rheumatic Arthritis. New York, Med. Record, 1866, No. 4.—*C. Hueter*, l. c., S. 108.—*J. Chéron*, Du traitement etc. Gaz. des hôp., 1869, No. 150, et seq.—*F. Hoppe-Seyler*, Ueber die Zusammensetzung von Flüssigkeiten, welche aus den Gelenken bei Arthritis deformans entleert wurden. *Virchow's* Archiv, 1872, LV., S. 253.—*J. Hutchinson*, Transactions of the Pathol. Society of London, 1872, XXIII., p. 195.—Verhandlungen der Berliner med. Gesellschaft., Sitzung vom 30 October und 13 November, 1872.—*Drachmann*, Arthritis def. Nordisk. Med. Arkiv, 1873, V., 1.—*A. Weichselbaum*, Arthritis def. der beiden Schulter- und Ellenbogen-gelenke und des linken Hüftgelenks. *Virchow's* Archiv, 1873, LV., Heft 1 u. 2—*E. Leyden*, Die Spondylitis deformans in Klinik der Rückenmarkskrankheiten. Berlin, 1874, S. 270.—*E. Rotter*, Arthritis deformans der Articulatio epistropheo-atlantica mit consecutiver Degeneration des Rückenmarks. Deutsches Archiv f. klin. Med., 1874, XIII., S. 403.—*Mor. Meyer*, Berliner klin. Wochenschrift, 1870, No. 22, u. 1873, No. 48.—*Althaus*, On the treatment, etc. Brit. Med. Journal, 1873, September 28.—The various manuals of surgery and morbid anatomy may likewise be consulted; also some of the books and memoirs enumerated under the head of Rheumatic Diseases and of Gout.

Introductory and Historical Observations.

The term *Arthritis Deformans* (arthritis sicca, spuria, nodosa, pauperum, rheumatoides, arthroxerosis, malum senile articulorum, rheumatismus nodosus, polypanarthritis [Hueter], rheumatic gout, nodular gout) is applied to a disease of the joints, causing chronic changes of an inflammatory kind that never issue in suppuration. It affects the nutrition of all the constituent parts of the joint, causing, on the one hand, abnormal proliferation, on the other, absorption; and so the whole shape of the joint becomes deformed.

No description of this disease can be found in the writings of the ancients. Even writers of a later date, including the present century (Morgagni, Sydenham, Cruveilhier), only allude to it incidentally, as one of the issues of "chronic rheumatism of the joints," or else confound it with gout. The disease itself is by no means a new one; the characteristic changes in the joints have been observed in skeletons dug up after they had long been buried. Thus della Chiaje, of Naples, has described traces of the malady in bones found among the ruins of Pompeii. Lebert[1] found bones similarly altered in the catacombs of Paris, and Virchow has recognized the disease in vertebræ dug up among the ruins of an ancient monastery in Pomerania.

The earliest notice of the independent character of the malady dates from the time when Landré-Beauvais in France, and Haygarth in England, wrote monographs describing the polyarticular deformity, implicating especially the smaller joints. At a later period, the Irish surgeons, W. Smith, Colles, and Adams, gave a full account of that variety of the disease which is almost exclusively confined to the greater joints, especially the hip; they called it *malum coxæ senile.* Anatomical inquiry, conducted chiefly in Germany (Rokitansky, Gurlt, Foerster, Fuehrer, Virchow, Volkmann), furnished proof of the identity of the local changes in all varieties of the disease. But those varieties are still, however, distinguished by their etiology and symptoms; hence the different views held as to their real nature, and the multitude of names conferred on the disease. This is now universally recognized as distinct from gout, for it is in no way connected with the peculiar dyscrasia that causes urates to be deposited in the joints. But there are many authors, especially in France and England, who regard the malady as a result of rheumatic influences, and class it among the chronic rheumatic inflammations of the joints ("chronic articular rheumatism"). But influences of this kind can only be assumed, with any degree of likelihood, to operate in producing that multiple form of the disease which attacks the smaller joints of the fingers and toes, and to which the descriptions of "rheumatic gout," given by those authors, do really apply. Indeed, the writers in question either leave that form of the disease which is most common in the aged—termed *par excellence malum coxæ* or *malum senile articulorum*—altogether unnoticed, or else they describe it separately. Others again describe the former as a polyarticular, the latter or senile kind as a monarticular—or, at any rate, oligarticular—variety of arthritis deformans. Inasmuch, however, as recent researches have shown that the latter form is very prone to implicate a considerable number of the intervertebral joints, and may therefore be likewise regarded as "polyarticular," this distinction between them is no longer tenable.

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[1] Handbuch d. prakt. Medizin. Tübingen, 1859, II., 874.

No rigorous line of demarcation between different forms of the malady can be drawn on the basis of the number and kind of joints affected; for, apart from that strictly localized variety which follows injuries inflicted on a single joint, and which possesses more of a surgical than a medical interest, all forms of the disease are alike in exhibiting a markedly *progressive* character, and are therefore either polyarticular, or on the way to become so. But though no distinction can be drawn from the *number* of joints affected, the *order* in which they are attacked furnishes useful data for our purpose. One form of the disease—that specially attributed to rheumatic causes, and known as "arthritis pauperum," "nodular gout," or "rheumatic gout"—usually begins in the fingers and toes, and gradually spreads, centripetally, to the larger joints. Another form, called by preference "senile," usually begins and reaches its utmost development in the joints of the trunk (vertebral column, hip), extending subsequently towards the periphery—the extremities. But even this distinction is not universally applicable; for arthritis deformans, in all its varieties, is mainly a disease of advanced life, when rheumatic causes may very well co-operate with senile degenerations. Hence it is by no means rare to find the two forms of the disease in combination, or passing into each other.

Etiology.

The peripheric variety of arthritis deformans,—that beginning in the smaller joints of the extremities—is much more common in women than in men, and is essentially a disease of the poorer class. Childhood and youth are almost entirely exempt from it; it grows more common towards the thirtieth year of life, and increases in frequency among women about the climacteric period. Prolonged exposure to cold and damp is one of the chief causes to which the malady is ascribed; but unfavorable hygienic conditions, inadequate food, debilitating influences such as hemorrhages, unduly protracted lactation, repeated pregnancies, grief and anxiety,—in a word, all the hurtful conditions to which the poor are especially exposed,—contribute to make the organism less capable of resisting the cause first mentioned. Finally, it seems worthy of notice that the joints usually selected by the disease are those which are most continuously and severely overtasked, *e. g.*, by manual labor (sewing, knitting, laundry-work, in women; watch-making, in men). Trousseau and Remak assert that in women the malady is frequently preceded by hemicrania.

That form of the disease which shows a tendency to pick out the larger rather than the smaller joints usually begins at a later period of life, and may, therefore, fairly be termed "senile." But we occasionally meet with exceptional instances of its commencement in middle life, especially in persons who are prematurely afflicted with other senile changes (atheromatous degeneration of the arteries, calcification, etc.). In marked contrast to the first variety, the present form of the disease is more common in the male than in the female sex, and attacks the rich no less than the poor. Thin people appear to be specially predisposed to it. Cold and damp, and the other debilitating influences enumerated above, appear to have less to do with its production.

It is only of recent years that attention has been drawn to the possibility that arthritis deformans and allied diseases of the joints may be of nervous origin; and existing observations seem to point exclusively to the former, peripheral variety of the disease, as connected with affections of the nervous system. Remak[1] and Benedikt[2] were probably the first to regard articular affections as a result of irritative states of the spinal marrow and sympathetic. Indeed, Remak went so far as to call arthritis deformans by a new name, "arthritis myelitica" and "myelitico-neurotica." Charcot and his pupils subsequently drew attention

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[1] Galvanotherapie der Muskel- und Nervenkrankheiten. Berlin, 1858, p. 413 et seq. Deutsche Klinik, 1863, No. 11.

[2] Ueber elektrische Untersuchung und Behandlung. Wiener Med. Halle, 1864, V., 14. See also Deutsch. Archiv für klin. Med. XI., p. 219.

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to the occurrence of peculiar articular swellings in locomotor ataxy and other forms of paralysis; and a considerable number of similar observations have since been put on record.[1] It is quite true that these articular swellings did not invariably present the characters of arthritis deformans; they often set in with abundant effusion into the joint, a symptom quite foreign to the latter disease; in other cases, however, the characteristic morbid changes developed themselves either at once, or after a time. Now, even if we admit that both these and other forms of joint-disease occurring in the course of nervous maladies are partly due to injury, to which the paralyzed limbs are of course more exposed than sound ones, still there are reasons why we should note the strikingly frequent coincidence of joint-affections with diseases of the central nervous system; for there are other grounds for thinking that the development of arthritis deformans is in some way influenced by the nervous system. I have already mentioned that grief and anxiety appear to have a hand in its production; and the influence of psychical causes is further illustrated by some cases recently published by Kohts,[2] in which the disease followed a fright. Again, the usually symmetrical order of its invasion and subsequent progress can hardly be explained unless we assume the existence of some central causes situated in the nervous system. The disease is often associated with neuralgic and tropho-neurotic symptoms. Finally, some results of treatment, particularly those recorded by Remak and others concerning the effects of electricity directed to the nerve-centres, serve likewise to support this view. On the other hand, when the structural alterations in the vertebral column are taken into consideration, we cannot deny the possibility of a totally different kind of connection between the nervous disorders and the joint-affection; the former might be viewed as *secondary* to the latter. The future must decide whether *primary* changes do really occur in the nerve-centres, and in which of the forms of arthritis deformans, if in any. For we can confidently assert, even with our present knowledge, that differences is this respect exist.

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[1] *Charcot*, Archives de Phys., 1868, I. 772.—*Fournier*, Union méd. 1869, 17.—*Ball*, Gaz. des Hôp. 1868, No. 128; Revue scientifique, 1872, No. 37.—*Charcot*, Des anomalies de l'ataxie locomotrice. Leçons recueillies par Bourneville, 1873.—*Ponfick*, *Westphal*, *Hitzig*, in Verhandl. der Berliner med. Gesellsch., loc. cit.

[2] Berl. klin. Wochenschrift, 1873, No. 24 et seq. Also *Leyden*, loc. cit., p. 159.

As regards the strictly monarticular, or rather "limited" form of arthritis deformans, it seems always to be brought on by local injury, which keeps up a slight but continued irritation of the joint, either directly or indirectly. Thus, for instance, we find the disease occurring as a consequence of continued pressure on the ball of the great toe by the boot, or of old-standing luxations or sprains, or of fractures in the neighborhood of or extending into the joints, and generally in connection with chronic inflammatory mischief in or about a joint. It is to the influence of such chronic inflammatory changes that we may fairly attribute those rare cases of arthritis deformans which are gradually developed in oldish people out of very prolonged rheumatic arthritis ("chronic articular rheumatism"). Such cases, in which the latter disease passes gradually into the former one, or is found associated with it, are chiefly to blame for the confusion that has prevailed between them.

Pathology.

Symptoms and Course.

The disease always comes on very gradually. Its earliest symptom is pain in one or more joints, appearing and disappearing without appreciable cause, or following changes in the weather or muscular exertion. The patients not unfrequently complain of a sense of lassitude in the joints, either from the very outset of the malady, or after the pains have lasted a short time.

The pains are often neuralgic in their character, radiating along the track of a particular nerve or through an entire limb. In the peripheric form of the disease they are usually situated in the finger and toe-joints, in the wrists and knees. In the more central or strictly senile form the pain is felt in the back, along the vertebral column, or in the hips, shoulders, and knees.

Gradually—*i. e.*, in the course of many weeks or months—the mobility of the articulations begins to be impaired ; they are a little stiff, the stiffness being greatest after prolonged repose, as when the patient wakes in the morning, and is only overcome by repeated movements. At the same time the articular ends of the bones become thickened. They are not tender, or but slightly tender, on pressure, and the skin over them is neither red nor painful. The extremities of the bones grow steadily larger as time goes on. They become displaced, owing partly to the change in their own shape, partly to other changes wrought in the joint by the morbid process. Attempts at movement are accompanied by a peculiar grating or crepitus, of which the patient is himself conscious, and which may be distinctly felt through the soft parts. Moreover, hard excrescences and nodular masses may not unfrequently be detected around the joint, which is greatly deformed by the combined effect of all these changes.

Early in the disease the soft parts in the immediate neighborhood of the joint, or even the entire limb, begin to waste ; the muscles especially exhibit a degree of atrophy which is very striking, and which—at any rate, in many cases—cannot be attributed to impaired mobility of the articulation, but must be viewed as a result of peculiar neuropathic or myopathic disturbances of nutrition. When the disease is more advanced, and the deformity is very great, the tendons also may be rigid and contracted. When the joints of the hand are implicated, we sometimes find fairly circumscribed and more or less painful thickenings, of variable size, in the soft parts of the upper arm or forearm. These thickenings may possibly be due to a circumscribed proliferation of connective tissue between the muscles, or perhaps, as Remak believes, to swellings in the course of the nerves ("*nodi neuritici*").

The spread of the disease may best be followed in the smaller, more peripheral joints. It is almost invariably symmetrical, as was pointed out by Budd and Romberg, and recently reasserted by Charcot. The other form of the disease, which selects the joints of the trunk, appears to obey this law of symmetrical evolution less strictly ; or it may be that symmetry is more easily traced in those joints which are more accessible to observation. The disease sometimes confines its ravages to the upper or to the lower half of the body. Drachmann's assertion that, when the hip-joints are involved, all the other joints escape, and *vice versâ*, is decidedly erroneous, for not only are the intervertebral articulations almost always affected in conjunction with the hip-joints, but it is far from unusual to find one or both knees, a shoulder, etc., simultaneously implicated. Moreover, when the patients are advanced in years, the joints of the trunk and those of the extremities may be attacked together, as I have already pointed out.

Of the different regions of the body, the hands are pre-eminently liable to exhibit a deformity which is absolutely characteristic. The fingers, usually from the index to the ring-finger, more rarely the little finger also, are flexed; the metacarpal ends of the first phalanges are dislocated towards the ulnar, less commonly towards the radial side. Similar changes take place in the carpal ends of the metacarpal bones. As a result of these alterations, the fingers are displaced and arranged in an imbricate fashion over one another, either towards the thumb or towards the little finger; the hand comes to resemble a bird's claw, especially when, as is not unusual, the hand itself is fixed in the attitude of extension. For the rest, there are many individual deviations from this type of deformity; these have been fully described by Charcot as special varieties. The thumb is usually spared, and remains freely movable, and, with its aid, the patient often learns to use his hands with great dexterity, notwithstanding the crooked state of the fingers. In the feet, on the contrary, the great toes are more frequently and more severely attacked than their neighbors.

When the disease affects the larger joints—the hip, knee, shoulder, or elbow—shortening of the limb is the most obvious of the effects produced; and the patient's limping gait, caused by the shortening of the thigh when the hip is the affected joint, forms one of the most important and constant of its symptoms.

The disease of the vertebral column (*spondylitis deformans*) in which complete ankylosis of the true joints, with formation of osseous bridges between contiguous vertebræ, is more common than in other regions, is chiefly characterized by great difficulty of movement or even complete rigidity of the spine, with pains radiating from the back. When the cervical vertebræ are affected, the patient is unable to bend or rotate his head; when the disease invades the dorsal or lumbar spine, the body is shortened and twisted. Moreover, the various irregularities in the vertebral canal may cause compression and irritation of the cord, of the nerves given off from it, or of the spinal ganglia; and it is to such accidents as these that some part of the frequent disturbances of innervation which have recently been attracting attention—viz., the shooting pains, paralyses, and trophic changes—may with some degree of likelihood be attributed[1] (p. 160).

Finally, cases occur in which all the joints of the body, those of the limbs as well as those of the trunk, the lower jaw, clavicle, etc., gradually become affected, and the patients drag on a miserable existence for years without being able to move.

The course of the malady, though exceptionally slow, is usually progressive. When once fully developed, it has never been known to recede of its own accord. Treatment exerts little influence upon it, and that only in recent cases. On the other hand, the disease often comes to a stop for long intervals of time. Many months or even years may elapse before fresh joints are implicated; and even in those already diseased the structural changes go on very slowly, with intervals of perfect quiescence, each exacerbation setting in with severe pain and some slight febrile disturbance. Apart from this, the malady runs its entire course without fever, and, roughly speaking, without severe constitutional disturbance, always excepting those rare cases in which the disease of the spinal column leads to secondary affections of the cord.

Repeated observations made by Drachmann showed that the amount of phosphoric acid in the urine was diminished (1.194 grammes in twenty-four hours instead of the normal quantity of 2.5 to 5.8 grammes). No other changes in the composition of the urine are known to occur.

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[1] Cf. *J. Bergson*, Zur historischen Pathologie der Brachialneuralgien. Berlin, 1860. *Virchow* (in his Archiv. and in Verhandl. d. Berlin med. Gesellschaft). *Leyden*, loc. cit. *Rotter*, loc. cit.

Morbid Anatomy.

The joint-affection is a chronic panarthritis, all the constituent parts of the articulation—cartilage, bone, and synovial membrane—being implicated in the inflammatory process.

In a fully-developed case of the disease, the articular ends of the bones are seen to be thickened and flattened out, with protuberant margins which overlap the diaphysis like projecting lips, and are studded with irregular bony outgrowths which are smooth and rounded rather than pointed. The cartilages are thinned and split up, soft and velvety in patches, and rough or villous; at many points they have undergone complete absorption, and the denuded surfaces of the bones are in contact with each other. The microscope shows the intercellular substance to be no longer uniformly hyaline, but fibrous and split up, while the cartilage-capsules are enlarged and filled with a number of corpuscles, many of which are undergoing fatty degeneration.

The mutual friction of the ends of the bones during movement of the articulation gives them a smooth and lustrous surface, traversed by delicate striæ, running parallel to the direction of movement, which are scratched by slight irregularities or detached osseous or cartilaginous particles. The bony sockets, intended to receive the heads of the bones (as in the hip and shoulder), are not unfrequently enlarged by this process of grinding; the head of the bone, indeed, may slip altogether out of its original place into a new socket thus made for it. Sometimes, again, the natural socket is narrowed and deepened by stout marginal protuberances, and the mobility of the head in it greatly impaired. The above changes are all limited to the epiphyses, whose tissue is rarefied throughout and osteoporotic in parts. It is only in the uppermost subchondral layer of the epiphysis that the mechanical irritation causes an overgrowth of bone-tissue; this layer accordingly acquires an ivory-like hardness.

The ligaments and inter-articular cartilages likewise are usually frayed out and more or less destroyed by fatty metamorphosis. The synovial membrane is thickened, and not very vascular as a whole; but its villous processes where it is reflected on to the bone are more vascular, longer, and more abundant than usual, giving it a spongy appearance; long filaments often project into the articular cavity. In rare cases, we find the capsule more or less ossified by thick, shapeless plates of bone projecting from the edge of the cartilage over the capsular ligament, so that the joint comes at last to be enveloped in a bony shell made up of separate pieces (Volkmann).

The contents of the articular cavity are nearly always diminished in amount. They consist, in the later stages of the disease, of a turbid, viscid, reddish yellow or reddish liquid, containing degenerated epithelial cells, scrapings of cartilage, and shreds of articular villosities. Loose bodies are by no means rare in the interior of the joints; they consist of bits of cartilage or bony outgrowths that have become detached.

Hoppe-Seyler has analyzed the fluid from the hip-joint in two cases of arthritis deformans. It was alkaline, clear after filtration, and furnished a clot on boiling—a clot partially soluble in water. In one case 1,000 parts of the fluid contained 942.72 of water, 23.19 of mucin, 20.92 of albuminoids, 0.93 of ether-extractive (cholesterin, lecithin, traces of oily matter), 1.3 of alcohol-extractive, 0.65 of water-extractive, 1.53 of acetic acid extractive, and 8.79 of inorganic matters. The large proportion of mucin is the chief point of difference between this fluid and normal synovia (Frerichs in Wagner's Handwörterbuch der Physiologie, III. p. 463.).

The soft parts about the joints—the tendons and muscles—may also be involved in the morbid process. The tendons and their sheaths, as well as the *bursæ mucosæ*, are often found ossified in old cases (the combined tendon of the psoas and iliacus is the most frequent seat of this change); sometimes the tendons are quite frayed out and thinned. The muscles may be more or less wasted and undergo degeneration into fat or connective tissue.

As regards the genesis of these changes, we may conclude that the disease of the articular cartilages stands foremost in importance, even though chronic inflammation of the synovial membrane may perhaps precede it in point of time. Volkmann regards the disease as essentially one of the cartilages; active proliferation takes place over their entire surface, though it is most marked at their free edges—those turned towards the synovial sinus; the cartilage-cells divide and multiply, and the intercellular substance, too, increases in quantity. Soon the overgrowth of the cartilage renders its free border more and more protuberant, and compels it to overlap the diaphysis. A progressive ossification of the newly-formed layers of cartilage sets in simultaneously in the deeper parts nearest the bone; and while the cartilage itself continues to furnish new material for ossification, the marginal protuberances are gradually converted into the tuberculated or nodular masses of bone already described. Hence these bony projections—so long, at any rate, as they continue to grow—are always coated with a thin layer of soft tissue which either is, or has been, cartilaginous. The enlargement of the articular ends of the bones by marginal excrescences cannot occur without displacement of the attachments of the capsular ligament, which nearly always coincide with the line where the cartilage joins the bone. Accordingly, the marginal excrescences carry the capsule with them as they grow. But this displacement of the capsule is often very irregular; folds or bands of the fibrous membrane dip down here and there between the protuberances and lead to the formation of pockets or diverticula, which often contain loose cartilages.

During this overgrowth and ossification of the articular cartilages, free scope is allowed for expansion at their margins; but where they are actually opposed to each other, the phenomena in question, though essentially similar in their nature, proceed at a far slower rate. Here, too, the cartilage undergoes proliferation; it may form warty prominences; its deeper layers become ossified, but, owing to pressure and mutual friction, the ossification of the deeper layers is sooner or later associated with decay of the superficial strata, which split up into fibres, or become fatty and are worn away; so the newly-formed bone comes at last to be denuded.

The atrophy of bone, which progresses simultaneously with the above phenomena of growth, does not consist, according to Volkmann, in a simple wearing away of the denuded articular surfaces. The process is, in the main, always *subchondral*, and consists in an inflammatory wasting of the bone-tissue.

The internal organs are found, on post-mortem examination, to present nothing more than the usual senile changes, or the residues of the intercurrent malady that carries off the patient. It is only in *spondylitis deformans*, as I have already stated, that we might expect to find *secondary* changes in the spinal marrow and its membranes, or in the trunks of the spinal nerves at the intervertebral foramina, or in the spinal ganglia, more immediately associated with the joint-affection. Such changes have actually been observed, as in Rotter's published case. In some forms of arthritis—related in some degree, at any rate, to the disease we are now considering—occurring in connection with locomotor ataxy, peculiar changes have been noticed in the cord besides those proper to the latter disorder; I allude especially to atrophy of the anterior horns or inflammatory swelling of the spinal ganglia; and these changes have been viewed as *primary*, *i. e.*, as the cause of the articular affection (Charcot). But this view wants more data to support it, especially as sufficient attention has not hitherto been paid to the condition of the vertebral column and its constituent parts in such cases.

Diagnosis.

Arthritis deformans cannot be certainly distinguished from many of its neighbors, especially from chronic rheumatic arthritis and the articular neuroses, so long as the characteristic deformities are still absent and the symptoms consist merely of pain and slight swelling of the joints. Nevertheless, the fact that the former of these two maladies—chronic rheumatic arthritis—is usually developed as a sequela of acute polyarthritis, may help us to arrive at a correct decision; while to distinguish arthritis deformans at this early stage from the articular neuroses there are scarcely any criteria, except the very uncertain ones derived from the possible predisposition of the patient to nervous affections in general. At a later period, when the deformity of the joints is once distinctly manifest, the diagnosis is easy, especially in the peripheric form of the disease, which begins in the smaller joints and extends symmetrically; with gout, indeed, it is scarcely possible to confound it. (See also *diagnosis* of gout, p. 129.)

The recognition of the other form of the disease, that which attacks the larger joints, is based on the age of the patient, the gradual onset and excessively sluggish course of the disease, the absence of fever, the stiffness of the joints, the grating that may often be perceived, the deformities and bony excrescences which are made all the more apparent by the wasting of the soft parts, the shortening of the limb, and finally, on the absence of any history of injury and the exclusion of other forms of joint-disease. Spondylitis deformans is characterized by much the same symptoms—the advanced age of the patient, the stiffness, shortening and curvature of the vertebral column, and the slow, apyretic progress of the malady.

Finally, there are cases of chronic rheumatic arthritis following acute articular rheumatism, which, after running a slow course, come ultimately to exhibit the deformity characteristic of arthritis deformans. It is chiefly to the existence of such cases, whose precise nature cannot always be ascertained, that the error of wholly identifying "chronic articular rheumatism" with "arthritis deformans" must be ascribed. In many such instances the two disorders merely complicate each other, and the likelihood of their doing so is very much increased by their being both brought on by much the same set of causes. In other cases, again, it is just possible that the chronic rheumatic arthritis may pass into arthritis deformans, *i. e.*, that a joint which has for a long time been suffering from the former affection may ultimately present the deformity characteristic of the latter (see also p. 152).

Duration and Issue. Prognosis.

The duration of arthritis deformans is only limited by that of the patient's life. The disease shows no tendency either to spontaneous recovery or to death. Accordingly, it usually goes on for many years, when the patient's life is not cut short by any intercurrent malady,—for ten, twenty, thirty years, or even longer. It sometimes lasts until extreme old age, causing no disturbance of the patient's general health save what is due to interference with his movements.

Hence, the prognosis—so far as danger to life is concerned—is by no means gloomy; but, as regards the chance of recovery, it is less hopeful. The purely senile form of the disease—that which begins in the joints of the trunk—is peculiarly inaccessible to treatment; on the other hand, the peripheric form has recently shown itself not unwilling to yield to appropriate remedial measures.

Treatment.

It is hardly necessary to speak of special prophylactic measures in connection with arthritis deformans, for of its proximate causes we know nothing, and the removal of the more general and remote conditions that favor its development is, for the most part, outside the proper business of the physician. When we have said that the ordinary rules of hygiene must be observed, we have said all there is to say; perhaps, indeed, we may lay special stress on protection against the weather.

When once the disease is established, treatment may be expected to do more for the peripheric than for the central or senile variety of the disease. Still, in the absence of anything better, the remedial measures I am about to suggest for the former may be employed for the latter variety likewise.

Of internal remedies, iodine has shown itself to be the most useful. It may either be given in the form of the tincture, as recommended by Lasègue (ten drops three times a day, in sugared water or in wine, gradually increasing the dose to a maximum of fifteen grains of iodine daily), or as iodide of potassium in solution, with or without the addition of small quantities of uncombined iodine, the dose being progressively increased with continual reference to the state of the patient's digestion. By following this plan for several weeks we often succeed in allaying the pain and also in reducing the amount of swelling to some extent; we may even check the onward progress of the disease for a considerable time. All other internal remedies which have been recommended (mostly the same as those which used to be given in chronic rheumatic arthritis) are as good as useless, and are certainly inferior to iodine.

Besides giving iodine internally, we may apply it outwardly, by painting over the swollen and painful joints. This must always be done with care, so as not to irritate the skin overmuch, for inflammatory irritants in the neighborhood of the joints tend rather to promote than to retard the morbid process going on in their interior (see p. 153). Hence, too, all powerful derivatives, such as blisters, etc., which are efficacious in many other forms of articular inflammation, should be avoided in the present one.

Among external remedies, electricity and warm baths are the best. In the hands of Remak, Flies, M. Meyer, Althaus, and others, the ascending continuous current has produced either relief or positive improvement. The positive pole of a battery of 10–15 elements is applied by a rheophore of small surface to the affected joints of the hands and fingers, while the negative pole is placed in connection with the forearm, at some little distance, by a rheophore of larger area. Galvanism of the cervical sympathetic has been found beneficial by many observers.

Warm baths, whether natural or artificial, should be employed just as they are in chronic rheumatic arthritis. The reader may refer to what I have stated under that head.

It is important, in all forms of the disease, to maintain the functional mobility of the affected joints, as far as possible, by means of active and passive movement. Absolute rest promotes stiffness of the joints, and may lead to the limb becoming fixed in some abnormal position, as well as to atrophy of the neighboring muscles. Special instruments have been devised (by Bonnet) to enable the patients to carry out passive movements in a systematic way without assistance. These instruments are described in works on surgery.

The treatment of arthritis deformans, when it is limited to one or to a few joints, is chiefly surgical, and need not, therefore, be discussed here.

RICKETS.

(Rachitis.)

LITERATURE.—*Joan. Baptist. Theodosius*, Epistolæ medicinal. 1554.—*J. Hollerius*, De morbis internis observ. 7. Lugduni, 1578.—*Barthol. Reusner*, Dissert. de talo infant. Basil, 1582.—*J. Schenckius*, Obs. med. de ossibus. lib. II. obs. 264. Frankofurti, 1600.—*Fernelius*, Universa medicina; de abditis morb. causis. lib. II. p. 166. Genevae, 1627.—*Dan. Whistler*, De morbo puerili Anglorum, quem patricio idiomate vocant: "The Rickets." Lugduni Bat. 1645.—*Theoph. de Garanciers*, Flagellum Angliae seu Tabes Anglica. Londini, 1647.—*Arnold Bootius*, Tractatus de affectibus (morbis) omissis. Pet. Borelli observ. med. Londini, 1649. Cap. XII.—*Fr. Glisson*, Tractat. de rhachitide s. morbo puerili, qui "The Rickets" dicitur. Londini, 1650; ed. II. 1660; ed. III. 1671. *Jv. Mayo*, (a) Tractatus duo, quorum prior agit de respiratione alter de rachitide. Oson, 1669. (b) Tractatus quintus de rachitide. Oson, 1674.—*Sachs*, Ephemer. nat. curios. annus primus, 1670, obs. 37.—*Pierre de Castro*, De membrorum et ossium mollitione. obs. 10, 11, 51.—*Van de Velde*, De rachitide. Diss. inaug., 1700.—*Joh. Storch*, alias *Pelarg*, Theor. und pract. Abhandlungen von den Kinderkrankheiten. Eisenach, 1750, III. S. 254.—*Joan. P. Buechner*, Diss. de rachitide perfecta et imperf. Argentorati, 1754.—*Duverney*, Traité des maladies des os. Paris, 1751, II. S. 321.—*Forbes*, in Copland's Dict. of Pract. Med., Vol. III.: "Rickets."—*G. E. Zeviani*, Tratata della cura dei bambini attachati della rachitide. Verona, 1761. (Historical investigation.)—*P. Lalouette*, An deformitates a rachitide oriundae machinamentis corrigi debeant. Paris, 1762.—*Jay*, Diss. de rachitide. Lugduni, 1762.—*Joan. Henr. Klein.*, Diss. sistens casum rachitidis congenitae. Argentorat., 1763, und Nova act. natur. curios. Vol. I. observ. 38.—*J. Mervin Nooth*, Diss. de rachitide. Edinb., 1766.—*Oetinger*, Diss. de viribus rubiae tinctorum antirachiticis. Tübing., 1769. *Hansen*, Diss. inaug. de rachitide. Götting., 1772.—*Leidenfrost*, Nonnulla de rachitide. Diss. Duis. 1771.—*Levacher de la Feutrie*, Traité du rachitis, etc. Paris, 1772.—*W. Farrer*, A practical account of the rickets in children, etc. London, 1773.—*J. Verardi*, Della rachitide. Napoli, 1875.—*Van Swieten*, Commentarii in Boerhavii aphor. Tom. V. (Historical disquisition.)—*De Magny*, Mémoire sur le rachitis, etc. Paris, 1780.—*Thomassin*, Journal de méd. chir. et pharm. XLIII. p. 222. 1775.—*Trnka de Krzowitz*, Historia rachiditis omnis aevi observata medica continens. Viennae, 1787. Deutsch, Leipzig, 1789.—*J. F. L. Cappel*, Versuch einer vollständigen Abhandlung über d. sog. englische Krankheit. Berlin u. Stettin, 1787.—*M. Haller*, De rachitide. Diss. inaug. Viennae, 1782, in Stollii Diss. Vol. I. Viennae, 1788.—*J. P. Franck*, Discursus

de rachitide acuta et adultorum. 1788, in his Op. méd. No. 10.—*Audibert*, Lettre à J. P. Franck, ibidem.—*R. Hamilton*, Remarks on scrofulous affections. London, 1791.—*E. F. G. Heine*, Diss. de vasorum absorbentium ad rachitidem procreandam potentia. Goetting, 1792.—*De Fremery*, De mutationibus figurae pelvis, etc. Diss. inaug. Lugduni, 1793.—*J. Veirac*, Abh. über die Rachitis oder englische Krankheit. Aus dem Holland. Stendal, 1794.—*A. Portal*, Observat. sur la nature et sur le traitement du rachitisme, etc. Paris, 1797. German transl. by Weissenfels, 1798.—*J. Cl. Renard*, Vers. die Entstehung und Ernährung, das Wachsthum und alle übrigen Veränderungen der Knochen zu erklären. Leipzig, 1803.—*Bolba* in Hufeland's, Harless' und Schreyer's Journal der ausl. med. Lit. Berlin, 1802. I. No. 2.—*Scarpa*, Anat. pathol. ossium in mém. de phys. et de chir. prat. Trad. de Leveillé. Paris, 1804.—*Kellar*, Diss. de ossium emollitione morbosa. Lugd. Bat. 1816.—*M. H. Romberg*, De rachitide congenita. Diss. Berolin, 1817.—*Stanley*, in Med. Chir. Transact. 1816. VII. p. 404.—*Howship*, ibidem VIII. p. 57.—*Giulani*, Sul rachitismo. Napoli, 1819. —*L. W. Ficker*, De rachitide morbisque ex ea oriundis. Berolin, 1821.—*Chr. Fr. Sartorius*, Rachitidis congenitae observatt. Diss. Lipsiae. 1826.—*F. M. J. Siebold*, Die englische Krankheit. Würzburg, 1827.—*Cruveilhier*, Bull. de la société anat. de Paris, 1828.—*F. Caruela*, Considerazioni sulla rachitide. Deutsch. Bonn. 1835.—*Rufz*, Gaz. méd. de Paris, 1834, Février.—*A. Shaw*, London Med. Gaz. 1835. XVI. and Med. Chir. Transactions. 1843. XXVI.—*G. H. Weatherhead*, A Treatise on Rickets. London, 1835.—*J. Guérin*, (a) Bull. de l'academie de médecine, 1837, 13 Juillet, Gaz. méd. 1839, No. 28–31. (b) Die Rachitis, from the French. Nordhausen, 1847. II. Aufl. 1862.—*Miescher*, De inflammatione ossium. Berolini. 1836.—*Ephraim* (*Remak*), Diss. Berol. 1842, and in Romberg's Klin. Ergebnisse, 1849. S. 96.—*Owen Rees*, Med. Chir. Transactions. 1838. XXI. S. 406.—*Richter*, Ueber das Wesen und die Behandlung der englischen Krankheit. Erfurt, 1841.—*Marchand*, Journal für pract. Chemie. 1842. XXVII. S. 83.—*Frerichs* in Annal. der Chemie und Pharm. 1843. XLII. 3. S. 251.—*C. L. Elsaesser*, der weiche Hinterhopf. Ein Beitrag zur Physiol. und Pathol. der ersten Kindheit. etc. Stuttgart und Tübingen. 1843.—*Lehmann*, Schmidt's Jahrbuch. XXXVIII. 1843. S. 280.—*Kuettner*, in Casper's Wochenschrift. 1843. No. 46 u. 47, and Journal für Kinderkrankheiten. XIV. 1856. No. 7 and 8.—*E. v. Bibra*, Chemische Untersuchung über die Knochen und Zähne, etc. Schweinfurt. 1844.—*Guersant*, Gaz. des hôp. 1846. No. 8–14. —*Sonntag*, De rachitide congenita. Dissertation. Heidelberg. 1841.—*Castagné*, Du rachitisme. Thèse. Paris, 1847.—*Gurlt*, De ossium mutat. rachitide effect. Diss. Berol. 1848.—*Trousseau*, Gaz. des hôp. 1848. Archives gén. de méd. 1849. Union méd. 1850, No. 77 seq.; Gaz. des hôp. 1851.—*Schulz*, Ueber Rachitis congenita. Diss. Giessen. 1849.—*J. Schlossberger*, in Archiv für Physiolog. Heilk. 1849. I. S. 68.—*F. W. Beneke*, Zur Physiol. und Pathol. des Phosphorsauren Kalks. Göttingen. 1850.—*H. Koelliker*, Mikrosk. Anatomie. 1848–49. II. S. seq. and in Mitth. der Naturforsch. Ges. in Zurich. 1849.—*Rambaud*, Nouvelles rech. sur le rachitisme. Revue méd. franc. et étr. 1852, Mars 16.—*P.*

Broca, Bull. de la soc. anat. de Paris. 1852.—*Beylard*, Du rachitis, de la fragilité des os, etc. Paris, 1852.—*H. Meyer*, in Henle und Pfeuffer's Ztschr. f. rat. Path. N. F. 1852. III. S. 143 and VI. S. 150.—*Virchow*, (a) in his Archiv f. path. Anat. IV. 1852. S. 307, and V. 1853. S. 409–507. (b) Cellular path. IV. Aufl. 1871. S. 505. et seq.—*Stiebel* sen. in Virchow's Hdb. der spec. Path. I. 1854. S. 528, and Rickets, Rhachitis oder Rachitis. Erlangen. 1863.—*Wedl*, Ztschr. der k. k. Ges. der Aerzte zu Wien. 1858. No. 11.—*Heinr Mueller*, Ueber die Entwickelung der Knochensubstanz in Ztschr. f. wissensch. Zoologie IX. S. 147 und Sep.-abdr. Leipzig. 1858.—*Bron*, Considér. sur les troubles digestifs et le rachitisme produits par la mauvaise alimentation chez les enfants à la mamelle. Paris, 1857.—*Mauthner*, Ueber acte Rh. Oest. Ztschr. für Kinderheilk. 1857. II. 11.—*Gouteux*, Du rachitis, etc. Paris, 1858.—*Al. Friedleben*, Beiträge zur Kenntniss der physical. u. chem. Constitution, u. s. w. in Jahrb. f. Kinderheilk. III. 1860. S. 61. u. 147.—*H. Krause*, De forma pelvis congenita. Diss. Vratislav. 1858.—*Liharzik*, Das Gesetz des menschlichen Wachsthums und des under der Norm zurückgeblieben Brustkorb u. s. w. Wien, 1858.—*Hauner*, Journal für Kinderkrankheiten, 1860. XVIII. 1.—*O. Weber*, Enarratio consumptionis rachiticae in puella. XXII. annorum observ. Bonn, 1862.—*G. Ritter von Rittershain*, Die Pathologie und Therapie der Rachitis. Berlin, 1863.—*Möller*, Acute Rachitis. Königsberger med. Jahrbuch. 1863. III. S. 135.—*Mayer*, Bemerkungen über Rachitis und den Nahrungswerth der Kalksalze. Aachen, 1866.—*Ruloff*, (a) Ueber Osteomalacie und Rachitis. Virchow's Archiv XXXVII. S. 434. (b) Ueber die Ursachen der fettigen Degeneration und der Rachitis bei den Füllen. Ibidem, XLIII. S. 367. —*L. v. Lewschin*, Zur Histologie des rach. Processes. Centralbl. f. d. med. Wiss. 1867, S. 593.—*B. Scharlau*, Ueber die sog. congenitale Rachitis. Monatsschr. f. Geburtsk. 1867, S. 401.—*A. Bruenniche*, Bidrag, etc., in Virchow u. Hirsch' Jahresber. 1867, II. S. 305.—*Bohn*, Beiträge zur Rachitis. Jahrb. von Kinderheilk. N. F. I. 1868, S. 194.—*Förster*, Fall von acuter Rachitis. Ebenda S. 144.—*Gee*, On Rickets. St. Barthol. Hosp. Reports, 1868, IV. p. 69 and p. 265.—*Tschoschin*, St. Petersb. med. Ztschr. 1869, XIV. 4.—*Schuetz*, Die Rachitis bei Hunden. Virchow's Archiv XLVI. S. 350.—*G. Wegner*, (a) Ueber Syphilis und Rachitis der Neugeborenen und den Zusammenhang beider u. s. w. Berliner klin. Wochenschr. 1869, No. 39 (Verhdlg. der Berliner Med. Gesellsch.). (b) Ueber hereditäre Knochensyphilis. Virchow's Archiv. L. S. 305. (c) Der Einfluss des Phosphor auf den Organismus. Ibidem LV. S. 11. LII. S. 359.—*Weiske*, Ueber den Einfluss von kalk- oder phosphorsäurearmer Nahrung auf die Zusammensetzung der Knochen. Zeitschr. für Biologie VII. S. 179 u. S. 333. X. S. 410.— *Fleischmann*, Das unregelmässige Zahnen, ein diagnostisches Hülfsmittel für beginnende Rachitis. Wiener med. Wochenschr. 1871, No. 50.—*J. S. Parry*, Observations on the frequency and symptoms of rickets. Amer. Jour. of Med. Sc. 1872, Jan. p. 17, and April, p. 305.—*H. Ritchie*, Clinical observations on rickets. Med. Times and Gaz. 1872, No. 9.—*N. F. Winkler*. Ein Fall von fötaler Rachitis. Archiv. f. Gyn. 1872. IV. S. 101.—

Strelzoff, Beiträge zur normalen Knochenbildung. Centralbl. f. d. med. Wiss. 1872, S. 449, and 1873, S. 273.— *Waldeyer* und *Köbner*, Beitr. zur Kenntniss der hereditären Knochensyphilis. Virchow's Archiv. LV. S. 367.—*Kehrer*, Zur Entwickelungsgeschichte des rach. Beckens. Archiv f. Gyn. 1872. V. S. 55. —*Taruffi*, La rachite. Rivista clinica. 1872, No. 5.—*H. Urtel*, Ueber Rachitis congenita. Diss. Halle, 1873.—*M. J. Parrot*, Sur une pseudo-paralysie causée par une altération du système osseux chez les nouveaunés, atteints de syphilis héréditaire. Archiv de physiol. norm. et path. 1872, No. 3–5. Deux cas des syph. héréd. avec lésions osseuses. Gaz. Méd. 1873, No. 44, and 1874, No. 4. —*H. Hirschsprung*, Den akute Rakitis. Hospitals Tidende, 1872, No. 27–28. —*E. Weiske* und *E. Wildt*, Unters. über d. Zusammensetzung der Knochen bei kalk- oder phosphorsäurearmer Nahrung (3. Abth.). Zeitschr. f. Biol. 1873. IX., S. 541.—*Heitzmann*, Ueber künstliche Hervorrufung von Rachitis and Osteomalacie. Wiener med. Presse, 1873, No. 14.—*Dusart* (*Laborde*), De l'inanition minérale et de l'influence du phosphate de chaux, etc., etc. Gaz. Méd. de Paris, 1874, No. 5 (Soc. de Biol.).—*F. Steudener*, Ein Fall von schwerer Rachitis. Deutsche Ztschr. für Chir. 1873. IV. S. 90.—*P. Bouland*, Recherches anat. sur le rachitisme de la colonne vertébrale. Comptes Rendus, 1874. LXXVIII. S. 564.—*Al. Fischer*, Ueber einen Fall von Rachitis Congenita. Archiv f. Gynäkol. 1874. VII., S. 46.—*G. Degner*, Ueber den angeblich typischen Verlauf der Rachitis. Jahrb. f. Kinderheilk. N. F. 1874. VII., S. 431 —*Klebs*, Arch. f. excep. Path. und Pharm. 1874. II., S. 425.—*L. Tripier*, in Dechambres, Dictionn. des sciences méd. IIIme. sér. I. 1874, S. 652, und Archives de physiol. norm. et pathol. 1874, S. 108.—*R. W. Taylor*, On certain peculiar swellings of the cranial bones, caused by rickets. Philadelphia Med. Times, 1875. No. 169, Jan. 23.—See also the various text-books on Surgery, Gynæcology, and the Diseases of Children.

Historical Introduction.

Rickets (*rachitismus*, *morbus anglicus*, *articuli duplicati*. *Zwiewuchs*, *Doppelte Glieder*) is a disorder of nutrition peculiar to childhood, which leads to overgrowth with deficient calcification of the tissues destined to form bone, and consequently to interference with the growth of the skeleton, with transient or permanent deformity of many of its constituent parts.

Our knowledge of rickets as an independent disease dates only from the middle of the seventeenth century, when its prevalence attracted the notice of English physicians, and led to its being thoroughly investigated by a committee specially appointed for the purpose (Glisson, Bate, and Regemorter), the result of whose investigations was published by Glisson in the year 1650.

There can be no doubt that the disease had been in existence long before this time, but it had not attracted attention. Stiebel asserts that an ancient statue of Aesop, the fabulist, exhibits deformities which show that he had suffered from rickets in infancy. Hippocrates is supposed to have alluded to rickets in his description of certain deformities (*De articulis*); similar allusions have been traced in the works of Galen, Celsus, and Zacutus Lusitanus. Still more distinct is the case described by John Baptist Theodosius, of a child seventeen months old, which suffered from extreme weakness, with curvature of the spine and ribs. Finally, the statements of Reusner, Formius, and Schenck leave no doubt as to the fact that in the sixteenth century rickets must have been far from uncommon in Switzerland, France, Holland, and Germany. Still, it does seem as though the disease had spread in an exceptional degree over England in the early part of the seventeenth century; at any rate, we know that it became a subject of interest about that time, and was discussed in monographs, among which that of Glisson, though subsequent in point of time to those of Whistler, Garancier, and Boot, excels its rivals in thoroughness and insight. Glisson himself thought the disease a new one, which—according to the result of inquiries set on foot by himself and his colleagues—made its first appearance in Dorsetshire and Somersetshire between 1612 and 1620. He gave it the name of "rachitis," partly because of the phonetic resemblance of this word to the vulgar English name of "rickets" (from the Anglo-Saxon ricq or rick, a hillock), partly because it pointed to the special deformity of the vertebral column (ῥάχις). When public attention had once been drawn to the disease, publications about it began to appear in all quarters of Europe, especially in Germany, and discussions set in concerning its true nature and cause. Some writers (Storch) contented themselves with the broad explanation that the disease consisted in a disturbance of the growth of the bones and muscles, owing to unequal distribution of the nutrient juices; others (Portal) were unwilling to recognize it as an independent disease, preferring to regard it as a symptom of various distinct maladies, chiefly of a dyscrasic order, such as syphilis, scorbutus, scrofulosis, arthritis, etc. Others, again (Hufeland), regarded it as a scrofulosis becoming localized in the osseous system, or as a syphilitic disorder (Boerhaave). Finally, the majority followed Glisson in considering it the same as mollities ossium, a view not without its adherents in our own day, among whom Trousseau and Lasègue, Stansky, Bouchut, Hohl, Beylard, may be enumerated. (Cf. Mollities Ossium.)

The rise of scientific chemistry towards the close of the last century, and the progress of normal and pathological histology, shed the first rays of light on the chemical and structural changes that occur in rickets, and on the way in which they differ from normal processes. The former branch of the subject was investigated by Fourcroy, Bolba, Rees, Schlossberger, Marchand, and Friedleben; the latter chiefly by Rufz, Koelliker, Broca, H. Meyer, Virchow, and H. Mueller. Virchow deserves special mention for having conclusively established the non-identity of rickets with mollities ossium.

Another step in advance was taken by Elsaesser (1843). He discovered the peculiar change wrought by the rachitic process in the skull, and gave it the name of "craniotabes." Lastly, we may allude to the experimental researches begun by Chossat and carried on by J. Guérin, with especial reference to the mode of origin of rickets, and repeated since that time by various inquirers pursuing the subject in different directions.

Etiology and Pathogeny.

Rickets is one of the most common of diseases, and exists in every quarter of the globe; it is most common, however, in cold and damp regions, such as England, Holland, certain parts of Germany and France. Unfavorable circumstances, want of light and air, contribute largely to its development. Hence, the disease is more common among the poor than among the well-to-do. It is especially abundant in great cities with a large proletariat, in densely populated quarters, in the overcrowded, ill-ventilated dwellings of the poor.

The following are some data concerning the relative frequency of the disease in different localities. Kuettner says that in Dresden 25 per cent. of all the children are rickety. At Prague, Ritter von Rittershain found 521 rickety persons among

3,875 brought to the polyclinic from 1860 to 1862, *i. e.*, 13.4 per cent. of all the out-patients (adults and children together); 1,623 of them were children under five, and of these 504, or 31.1 per cent. were rickety. At Copenhagen, on the other hand, Bruenniche observed only 163 rickety children (6.3 per cent.) among a total of 2,595, from 1862 to 1867; and among a residue of 1,883 children, after exclusion of those above five years of age, 159, or 8.4 per cent. In London, Gee found only 2.36 per cent. of the in-patients at the hospital for sick children rickety, while the proportion of rickety subjects among infants under two years of age amounted to 30.3 per cent. At Manchester Ritchie met with 219 (30.3 per cent.) rickety children among 728 out-patients. In Philadelphia, Parry found 28 per cent. of all the children under five showing signs of the disease. The register of out-patients at the University Polyclinic of Berlin for the summer session of 1870 gives 80 cases of rickets among 665 children (12 per cent.); in the summer of 1871, 126 cases among 1,000 (12.6 per cent.); from October, 1871, to the end of December, 1872, 355 cases among 3,266 (10.9 per cent.); during the year 1873, 295 cases among 2,764 (10.7 per cent.). The total number of 7,695 sick children thus furnished 856 cases of rickets, *i. e.*, 11.1 per cent. If we deduct all the children over five years of age, we find that 650 cases of rickets were observed among 4,715 patients (13.8 per cent.) between Oct., 1871, and the end of 1873.

The period of the first dentition (from the sixth to the thirtieth month) is the usual time for the appearance of rickets. It then becomes gradually less frequent till the fifth year of life; between the age of five and puberty it is quite an exceptional phenomenon.

The disease is sometimes developed *in utero;* in such cases it may be found, at birth, to have already run its course (fœtal rickets), or it may progress after the child is born (congenital rickets, after Winkler). The latter variety—congenital rickets—likewise includes those cases which exhibit the changes in the bones—the swelling of the epiphyses—very soon after birth, during the first few weeks, for in such cases the tendency to the disease, and even its origin, must undoubtedly be referred to the intra-uterine period of life. Still, although the existence of fœtal and congenital rickets cannot be denied (as has been done by Boerhaave, Van Swieten, Zeviani, and others), we must be careful how we include in this category many cases originally assigned to it by Glisson, Storch, Morel,[1] Klein, and many other writers down to our own time; for many deformities of the skeleton met with in the fœtus and the new-born infant used to

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[1] *S. Vandermonde*, Recueil périodique. VII. 1757, 7 Juillet, p. 434.

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be set down, particularly by the older observers, as due to rickets; whereas we have every reason to believe that they were either certainly or very probably due to diseases of the bones of a wholly different kind (B. Scharlau, Urtel).

Again, many observers claim to have seen rickets begin even *after* puberty, though before the development of the skeleton is complete (up to eighteen or twenty in the female, and twenty-two to twenty-five in the male sex). Thus, Glisson mentions two cases between sixteen and seventeen; Portal, five cases between fifteen and eighteen. Ollier considers certain curvatures of the spine, developed in subjects not previously rachitic, about the age of seventeen or eighteen, as the expression of a rachitic tendency (*rachitisme tardif*); and Tripier adds five cases in which swellings on the upper and lower extremities made their appearance in young men. Meanwhile, all the above cases, and, indeed, the very occurrence of rickets after puberty, must be considered doubtful so long as the specific character of the changes in the bones has not been proved by microscopical examination.

The following figures illustrate the comparative frequency of rickets at different ages:

Guérin's Statistics.

Before birth	3
During the 1st year of life	98
“ “ 2d “ “	176
“ “ 3d “ “	35
“ “ 4th “ “	19
“ “ 5th “ “	10
From the 6th to the 12th year of life	5
Total	346

Von Rittershain's Statistics.

During first six months of life	91
“ second “ “	175
From 1 to 2 years	154
“ 2 “ 3 “	62
“ 3 “ 4 “	15
“ 4 “ 5 “	7
“ 5 “ 9 “	17
Total	521

Bruenniche's Statistics.

During first half-year	1
“ second “	19
From 1 to 2 years	79
“ 2 “ 3 “	47
“ 3 “ 4 “	7
“ 4 “ 5 “	6
“ 5 “ 8 “	4
Total	163

Ritchie's Statistics.

During first half-year	7
“ second “	65
From 1 to 2 years	109
“ 2 “ 3 “	25
“ 3 “ 4 “	9
“ 4 “ 5 “	4
Total	219

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Many authors believe in the influence of sex, while others contest it; but the statements of the former are so little in harmony with one another, that we may fairly conclude that there is no great difference between the sexes as regards their liability to rickets.

Guérin gives 148 boys to 198 girls; Ritter von Rittershain, 290 boys to 231 girls; Bruenniche, 108 boys to 55 girls; the proportion between the sexes in the total number of patients seen being nearly equal (1,337 boys to 1,258 girls). Ritchie gives 128 boys to 91 girls. Dufour found the number of rickety girls fifteen times, Marjolin twenty times, as great as that of rickety boys.

Hereditary influence may be traced with certainty in many cases of rickets. The tendency is most often inherited from the mother, traces of previous rickets being less often observed in the father of rickety children. There are families in which all or a majority of the children become rickety without our being able to ascribe the malady to any external noxæ of a uniform kind. On the other hand, it has been noticed that in two or more families, living under the same roof and in exactly the same way, only those children became rickety whose father or mother had previously suffered from the disease. The influence of inherited predisposition is further illustrated by many cases of fœtal or congenital rickets for which no other cause, such as syphilis or disease of the placenta, could be made out. Of course, when causes of the latter kind are in operation, the case is not one of true inherited rickets, but of rickets acquired *in utero*.

Other constitutional maladies in the parents may likewise contribute to produce rickets in the offspring, especially, as appears from the evidence collected by Ritter v. Rittershain, chronic tuberculosis in the father. He found seven tuberculous fathers and four tuberculous mothers among the parents of seventy-six rickety children whose family history he was able to investigate. Again, constitutional syphilis in the parents is a cause of rickets in the children; but its influence is far smaller—at least, on the ordinary form of the disease which sets in during teething—than the authority of Boerhaave (*Aphorism*, § 1482) might lead us to suppose—perhaps, because the children of syphilitic parents usually die, either *in utero* or very soon after birth. When they survive, they seldom fail to have rickets. On the other hand, it has been shown by Wegner, and subsequently by Parrot, Waldeyer, and Koebner, that those children of syphilitic parents who die early constantly exhibit morbid peculiarities in the growth of their bones, in addition to the specific lesions of syphilis—peculiarities closely analogous to those met with in extra-uterine rickets. Hence, it must still be left an open question whether syphilis should be considered the most effectual cause of intra-uterine rickets, or whether—perhaps more justly—the bone disease should not rather be viewed as a specific result of syphilis, wholly distinct from rickets. It is probable that many of the cases of so-called rickets, developed during the earliest stages of life, were really instances of syphilitic disease of the bones.

Finally, debility from whatever cause, anæmia, chronic discharges, enfeebled nutrition in one or both parents, advanced age at the time of procreation, may all promote the development of chronic disease in general, and of rickets in particular, in the offspring.

Among exciting causes improper feeding takes the foremost place. Its importance was known, in a general way, even to Glisson and his contemporaries. Subsequently, however, J. L. Petit's view became popular, and it was thought that early weaning formed the principal cause of rickets. Petit taught that to prevent rickets it was necessary to keep the infant at the breast till all its teeth had cut the gums. Zeviani, however, was not without adherents in the belief that rickets was brought on by precisely the opposite error, viz., by keeping the child at the breast for too long a time. Both views are to a certain extent legitimate. The evil does not lie in the mother's milk (supposing its composition to be normal), but in the fact that when the infant is prematurely weaned the nourishment substituted for the mother's milk is unsuited to its digestive powers and the requirements of its organization; while, on the other hand, when it is kept too long at the breast the milk alone becomes insufficient for its nourishment. At the present time it seems more necessary to insist on the latter than the former of these considerations; for the agitation which has been carried on, and rightly carried on, by physicians against the premature weaning and artificial feeding of infants, has recently led, at any rate in Berlin, to an error of an opposite kind in the minds of a large number of the public. They have been led to believe that an infant cannot be restricted too long to the milk of its mother or of a wet-nurse. Indeed, in the rural districts (of Germany) a large —perhaps the larger—proportion of all the cases of rickets is furnished by children who have been kept at the breast till they are a year old, or even older, without being supplied with any additional nourishment, or at most with extremely little of it.[1]

But it is not the particular kind of food, nor any special quality or constituent of it, that causes rickets. Any diet unsuited to the child's age and the state of its development will bring on rickets, as is proved by the occurrence of the malady in children fed in the most divers ways. Attempts have been made to prove experimentally the power of unsuitable nourishment to generate the disease in the growing organism. Guérin took puppies away from their dam and kept them on a meat diet. They are said to have shown all the signs of rickets in its most typical form after four or five months of this treatment, while other puppies of the same litter, suckled in the usual way, remained in good health. But a more recent series of experiments conducted by L. Tripier on cats, dogs, and chickens has proved that while such unsuitable feeding may undoubtedly cause the death of any of the animals subjected to it, it fails to induce true rickets. Others, again, setting out from the fact that the bones of rickety children are less rich in mineral constituents—especially lime and phosphoric acid—than normal bones (*vide infra*, p. 187), have tried to lay the blame on a want of those constituents in the food supplied. They refer to the experiments of Letellier, von Bibra, Chossat, and Milne-Edwards, junior;[2] Chossat having produced deformity of the bones in pigeons, and Milne-Edwards in dogs, by feeding them on a diet deficient in phosphoric acid and the salts of lime. Here again, as Friedleben proved by repeating Chossat's experiments and making a careful analysis of the bones, true rickets is not produced; there is merely a diminution in the earthy constituents of the bone-tissue, and the resulting fragility of the bone is entirely passive and due to atrophy. Moreover, it is very doubtful if we can ever reduce the proportion of lime and phosphoric acid in the bones, even of rapidly growing animals, by withdrawing these compounds from their food (Weiske); for the accurate analyses of Weiske and Wildt have proved that even under such conditions the bones may retain their normal chemical composition. Lastly, even the experience of veterinary surgeons and agriculturists (Roloff), that young animals pastured on soils which are poor in lime are liable to suffer from rickets, does not go for much; for the consentaneous operation of other causes is not excluded, and there exist counter-observations to prove that rickets may be developed even apart from any lack of lime-salts in the food (Schuetz).

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[1] The chief reasons why infants are kept as long as possible at the breast among the lower orders are: first, the convenience and cheapness (?) of this mode of feeding them; secondly, the prevalent belief that lactation protects the mother from the risk of renewed pregnancy. Among the wealthier classes there is the added dread of the child's becoming restless; when a wet-nurse is kept, her personal interest tells the same way, and induces her to avoid habituating the child to other nourishment, etc.

[2] Vide *Kühne*, Lehrbuch d. physiolog. Chemie, 1868, p. 397.

We may therefore conclude that a deficient supply or deficient absorption of lime and phosphoric acid is not, *per se*, capable of inducing rickets. Besides, cow's milk and farinaceous substances, the common substitutes for mother's milk, are not by any means deficient in lime and phosphoric acid. The causes of rickets must be looked for elsewhere, and we must acknowledge that a deficiency of lime in the bones is not the *primary* fact in the disease. Minute anatomy has long since shown that the essence of the rachitic process does not consist in a mere diminution of the earthy salts in the bones, but far more in an irritation of the osteoplastic tissue. Wegner, moreover, has recently brought experimental evidence to show that true rickets may be artificially produced by the continued administration of very minute doses of phosphorus (which exert a specific irritant influence upon the osteoplastic tissue), together with a simultaneous withdrawal of lime from the food. We may fairly assume, therefore, that some irritant matter endowed with the same properties as phosphorus is either introduced into the body with the unsuitable food, or else generated from it in the system (the latter being the more plausible hypothesis); further, we must suppose either that the food is deficient in lime, or that the absorption of lime-salts from the alimentary canal is in some way hindered. Should the statements recently put forth by Heitzmann be confirmed, our comprehension of the mode in which improper feeding may cause rickets will be greatly facilitated. Heitzmann asserts that lactic acid influences the osteoplastic tissues—at any rate, in carnivora—in exactly the same way as phosphorus, and that, when combined with a deficiency of lime in the food, it is capable of inducing true rickets. Now, there is certainly no want of opportunity for the formation of lactic acid in the alimentary canal of an infant. The milk and arrow-root, the meal and potato-pap, and other farinaceous compounds that are commonly substituted for mother's milk, will furnish any quantity of lactic acid, especially when a gastro-intestinal catarrh is already present, or is brought on by the improper nourishment itself. One of the two conditions which Heitzmann considers necessary for the development of rickets would thus be fulfilled. That lactic acid in excess is really present in the system of rickety infants may be inferred from its having been detected in their urine by Marchand, Lehmann, and Gorup-Besanez.[1] The other condition—inadequate supply or inadequate absorption of lime—may readily be fulfilled whenever the mother's milk, owing to protracted lactation, or constitutional feebleness, or advanced age, becomes poor in earthy salts, or whenever disturbances in the digestive apparatus of the infant cause those salts to be excreted more abundantly than usual. Here are facts in support of both the above alternatives. It has long been known, and has been conclusively proved by Vernois and Becquerel, that the proportion of salts in human milk diminishes progressively after the age of twenty, and also after the sixth or seventh month of lactation. Further, we know that an abnormal quantity of salts is removed from the body by diarrhœa, and there can be no doubt that among those salts are the calcareous compounds taken in with the food.

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[1] Lehrbuch der physiolog. Chemie. 1867. p. 523.

Moreover, the only published analysis of the fæces of a rickety patient[1] actually shows a very high proportion of ash (twenty-three per cent.), consisting of phosphates, principally in the form of bone-earth. The abnormal excess of phosphate of lime in the urine of rickety children cannot be taken as proof that the amount of lime absorbed from the alimentary canal is not diminished, for the fact in question may be readily explained by the solvent capacity of the lactic acid in the system for the lime-salts already deposited in the child's skeleton (cf. Mollities Ossium).

To sum up: the morbid process which underlies the development of rickets may, in accordance with the results of experiment and the clinical observations we possess, be explained in the following way. Owing to digestive disturbance, either pre-existent or brought on by improper feeding, lactic acid is generated in the system; this operates, on the one hand, as an irritant on the osteoplastic tissues; on the other, as a solvent on the calcareous salts deposited in the bones, promoting their elimination. At the same time the supply of earthy matter is reduced, either directly (as in cases of protracted lactation) or indirectly (as when diarrhœa carries off the lime-salts from the intestines before they are absorbed).

It is not impossible that other substances, capable of irritating the osteoplastic tissues, may exist (besides phosphorus and lactic acid), of which we know nothing. To their influence we may attribute those very rare cases of rickets which are developed in consequence of hereditary predisposition, without marked digestive disturbance or improper feeding. No other explanation of such cases can be offered, or of those in which rickets is induced *in utero*, either by hereditary syphilis or by local disease of the placenta, or by unknown causes. We are driven to suppose that in all these instances the irritant which excites the abnormal overgrowth of the osteoplastic elements is developed from some morbid state of the blood and humors; further, that the products of proliferation interfere with the deposition of the earthy salts in the bone, or that they are incapable of taking up those salts. For, so far as we can judge from the experimental data furnished by Wegner and Heitzmann, the irritation of the osteoplastic tissues would not of itself lead to rickets, without a simultaneous diminution in the supply of lime. It may be that the substances which hinder the deposition of the earthy salts are organic acids (formic, acetic, lactic, etc.); for young bone-tissue, so far as our scanty information concerning it will enable us to judge, is as prone to the formation of such compounds as the splenic tissue, to which it is in many ways so nearly allied. We know that the spleen in certain hyperplastic states (leukæmia) generates acid in excess; we are allowed to speculate that a similar formation of acid may take place in growing bone-tissue—of acid capable of dissolving the earthy salts—and formed in such abundance as actually to prevent the calcification of the new tissue, unless a proportionate excess of earthy salts be simultaneously introduced into the system.

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[1] *Klecinsky* in *Ritter* v. *Rittershain*, loc. cit. p. 38.

Pathology.

General Outline of the Disease.

Rickets comes on very insidiously. Its earliest symptoms are not characteristic, so that it is difficult to fix the precise time of its beginning. They are usually connected with the digestive apparatus: irregularity of the bowels, frequent diarrhœa, acid eructations and vomiting, tympanites, etc. The child is restless, pale, and sickly; it often shows unmistakable signs of wasting, and cries when its limbs are firmly grasped or when it is raised by putting the hands under its arm-pits. Bronchial catarrh is a frequent complication; febrile symptoms may set in, as restlessness and heat of skin towards evening and through the night, subsiding towards morning with an outbreak of perspiration. Even without much sign of fever the child is often bathed in perspiration, especially about the head and upper part of the chest. When no cause can be made out for these symptoms, and they coexist with the digestive disorders alluded to above, they may be allowed to stand for indications of commencing rickets. It is not till they have lasted for some time that the characteristic irregularities in the growth of the bones make their appearance; sometimes, though very rarely, the deformities in the skeleton may show themselves in children otherwise well nourished, during the second or third year of life, without any such prodromata, and, indeed, without any appreciable disturbance of the general health. Moreover, similar deformities have, in a few instances, been observed to appear quite suddenly; such cases have been described under the name of "acute rickets." (*Vide infra*, p. 183.)

The rachitic changes may occur in every bone in the body, but the resulting deformities and functional troubles vary according to the patient's age and the degree of development previously attained by his skeleton. The articular ends of the long bones swell and protrude under the soft parts that cover them, more especially in the hands, feet, elbows, and knees. The prominence of the contiguous epiphyses, between which the articular cavity itself forms a depression, has given rise to the term *articuli duplicati* (*Zwiewuchs*). In the skull the disease shows itself by delaying the ossification and closure of the fontanelles and sutures; the bones themselves, particularly the occipital bone, are soft and flexible in parts, where they may often be depressed by the finger as though they were made of parchment. In conformity with the age of the child, teething may either be checked and proceed in a slow and irregular way, or the teeth which have already cut the gum are arrested in their growth, become discolored and brittle, and finally drop out. The force applied to the softened bones by the muscles attached to them and by the weight of the body, leads to further deformity of the trunk and limbs, mostly by causing willow-stick fracture of the long bones. The legs usually exhibit an outward curve and become scimitar-shaped; the fore-arms are bent in a much slighter degree towards their flexor aspect. The thorax is characteristically distorted. The junctions of the ribs with their cartilages become thickened and nodular; they may be seen and felt on the side of the chest, like a chaplet of beads curved with its concavity outwards (rickety rosary). The ribs are laterally compressed *en masse*, making the breast-bone project like the keel of a boat. The sides of the chest are sucked in with every inspiration, especially when, as so often happens, there is catarrh of the air-passages; the upper part of the abdomen (epigastric region) is simultaneously protruded, and when the *besoin de respirer* grows more intense, a deep groove (Harrison's groove) makes its appearance between it and the thorax during every inspiration—a groove that corresponds to the line of insertion of the diaphragm.

There is often spinal curvature. It usually begins as a kyphosis, which may subsequently become complicated with skolioses. Finally, the pelvis may also become deformed, the pubic bones being usually thrust towards the sacrum.

The increase in length of the body as a whole is delayed. The child cannot be taught to stand or walk alone; or, if already able to walk, it loses the faculty of doing it. It is unwilling, particularly at the outset of the disease, to put its feet to the ground—perhaps from dread of pain, perhaps from a sense of weakness. When the child does attempt to walk, its gait is tottering and awkward, and it is soon weary. In marked contrast to the delayed growth of the trunk and limbs, the hairy part of the head, whose growth is unchecked, seems unduly big and often sinks down between the shoulders; the abdomen, already swollen by the gastro-intestinal mischief, seems even more prominent in relation to the shrunken thorax. In advanced cases of the disease the child looks like a dwarf; its mind is often well-developed, or even precocious (this is especially the case in older children, in whom the digestive disturbances are less severe; younger ones are usually cross and sluggish, and are best satisfied when allowed to lie motionless in bed, or to squat on their nurse's arm).

The disease does not always advance very far. The structural changes are often limited to a few only of the bones, and stop short of complete softening of their tissue; the pain and functional disturbance may be insignificant; the morbid process is soon checked, the bones consolidated, trifling deformities set right by renewed activity of growth, digestion and nutrition restored, and the disease brought to a close in a few months, leaving only slight thickening of the affected bones behind. This mild form of the disease usually occurs in children whose digestion has never been greatly disturbed, and whose nutrition has never fallen to a very low ebb, *i. e.*, in older children of the well-to-do class. And even when the disease does extend farther in such children, its extension takes place very slowly, with intermissions lasting weeks or even months; the morbid changes are inconsiderable, and the process terminates at last in recovery, just as in the previous instance, only leaving a somewhat larger number of more or less striking deformities behind it.

But when the digestive disturbances are very marked and obstinate, and the surrounding circumstances of an unfavorable kind, the morbid changes in the bones are usually more severe, the patient's strength gradually fails, the wasting becomes extreme, and death ensues just as in chronic catarrh of the intestines with the symptoms of marasmus and hectic fever.

There are other cases of rickets in which the prominent symptoms are exhibited by the respiratory apparatus. The weakly infant, with its diminished power of resistance to cold, suffers greatly from bronchitis, which may assume a serious aspect, owing to the deformity of the chest and spine already referred to, and the resulting interference with the respiratory movements; or the bronchitis may pass into lobular collapse or broncho-pneumonia. Lastly, the softening of the cranial bones renders the child liable to disease of the brain and its membranes, the skull not offering sufficient protection against injury from without.

Any one of the above-mentioned forms of rickets may be attended with fever; but the fever seems rather to depend on the patient's general state, upon the complications and sequelæ of the disease, than upon the actual changes in the bones. Still, the connection between the bone-mischief and the other morbid conditions is undoubtedly close; for the rate at which the former progresses determines the degree to which the other disorders and the febrile symptoms attain, and *vice versâ;* so that, in the more acute form of rickets, occurring in children about twelve months old, and almost invariably preceded and accompanied by gastro-intestinal catarrh, it remains a question whether the actual rachitic process may not have some share in exciting the febrile symptoms that are present.

This view is further supported by those very rare cases to which I have already alluded under the name of "acute" rickets, by way of distinction from the ordinary more chronic variety of the disease. Feist[1] seems to have been the first to draw attention to this form; Moeller, Hauner,[2] Bohn, Foerster, Hirschsprung, have recorded similar cases, and I have myself seen one. Within a few weeks the epiphyses of all or most of the long bones become swollen, there are swellings on the cranial bones likewise, and these phenomena are accompanied by fever. In several of the recorded cases there was simultaneous swelling of the gums and palate, together with disturbance in the digestive functions. The cases hitherto observed occurred in children between four and sixteen months old, usually well nourished, and placed under comparatively favorable conditions; occasionally, however, the symptoms broke out in children already much reduced. In the latter set of cases death followed the development of complications (pneumonia), but in the former series—a majority of the whole number—the disease ran its course within a period of a few weeks, and ended in complete recovery. In several instances recovery was followed by a very marked activity of growth.

The case that came under my own observation was that of an infant four months old, whose health had previously been good. It had been fed, and had thriven on Nestle's food for infants. In January, 1873, a sharp febrile attack ushered in swelling, first of the lower end of the humerus, then of the lower epiphyses of the radius and ulna, of the tibia, fibula, and femur, on both sides of the body. The swelling was not in the joints, which remained perfectly movable; it was limited to the epiphysis, and the swollen part subsided very gradually into the diaphysis. The skin was not reddened, but the swollen ends of the bones were somewhat tender on pressure. There was an entire absence of constitutional disturbance, apart from the febrile symptoms. In about six weeks, without any active treatment, the swellings subsided completely, the fever having previously disappeared. I have not seen the patient since.

There can accordingly be no doubt that about the period of the first dentition children are liable to suffer from acute multiple enlargement of the epiphyses and sub-periosteal swelling of the bones, similar to those in ordinary rickets; these changes cannot be traced to any but constitutional causes, and must, therefore, be regarded as truly rachitic. But as no minute investigation of the bones has hitherto been carried out in any of the few cases of this kind that have ended in death, strict proof is still wanting of the identity of the morbid changes in question with those that are characteristic of genuine rickets.

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[1] Zeitschrift für Geburtsk. V. p. 101.

[2] Jahresbericht u. s. w. in Journal für Kinderkrankheiten, 1867, XLIX.

Morbid Anatomy and Chemistry.

Rickety bones, when the disease is at its height, show distinct signs of morbid change, even to the unaided eye. The long bones are greatly thickened at their epiphyses, less so in their diaphyses; they are unnaturally pliant; they are more easily cut with the knife than healthy bones at the same stage of development. On longitudinal section, the entire bone appears intensely congested; the medulla, the periosteum, and the subperiosteal tissue are deeply reddened, and as if soaked with blood. But the most striking of the alterations are situated at the junction of the epiphysis with the diaphysis.

In the normal epiphysis of a growing bone several distinct layers may be made out with the unaided eye. In their order from the extremity of the bone towards its diaphysis they are: 1. A milk-white zone of ordinary cartilage, consisting of an extensive hyaline matrix, in which the cartilage-cells are embedded, first in rows parallel with the articular surface, then in roundish groups. 2. The "zone of proliferation," 1–2 mm. deep, of a bluish white color; here the matrix sinks into the background, the corpuscular elements divide and multiply, and then array themselves in columns parallel with the long axis of the bone; the youngest elements, moreover, increasing in size (hyperplastic and hypertrophic zone of Strelzoff,[1] Klebs,[2] v. Brunn[3]).

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[1] Loc. cit.; also in Untersuchungen aus dem. pathol. Institut zu Zürich, herausg. von *Eberth*, 1873, Heft I. p. 52.

[2] Loc. cit., p. 434.

[3] *Reichert* u. *Dubois-Reymond's* Archiv, 1874, p. 1.

3. A narrow strip, of a grayish or dull yellow tint, $\frac{1}{8}$–$\frac{1}{2}$ mm. in depth, which passes directly into the spongy bone-tissue. It is here that those final changes occur in the cartilage which pave the way for actual ossification, those changes consisting in the penetration of vascular loops, the appearance of medullary cells and osteoblasts, the partial liquefaction of the matrix, and the precipitation of earthy salts in what is left of it. Next to this layer comes the true bone-tissue. The minuter phenomena of this last stage in the process are still under discussion. Concerning the origin of the osteoblasts, more especially, there are two opinions: one (upheld by H. Mueller in some degree, by Gegenbaur, Koelliker, Stieda, Strelzoff) regards them as new elements substituted for the cartilage-cells—as emigrant leucocytes, in short; the other (upheld by Virchow, Waldeyer, Klebs, von Brunn, Ranvier[1]) looks upon them as the direct progeny of the cartilage-cells. All these metamorphoses—the proliferation and expansion of the cartilage-cells, the calcification, the advance of the medullary spaces and vascular loops at the limit of calcification, and the final ossification—are normally accomplished with the utmost uniformity in the successive layers. Hence, in a longitudinal section of the bone, the boundary between any two of the layers is always a straight line.

Now, in rickets we find: 1. The zone of proliferation developed in excess, from five to ten times as wide as it ought to be; the zone of calcification lying next it is also inordinately wide, and has a perforated, sieve-like appearance (spongoid tissue of Guérin). 2. These two layers are not separated as usual by a definite line (which appears straight in longitudinal sections), but interpenetrate each other in an irregular way; so that we not unfrequently come across grayish white or yellowish promontories and islets of calcified tissue in the midst of the bluish and translucent zone of proliferated cartilage-cells. 3. The medullary spaces are not confined, as in normal bones, to the limit of calcification; they penetrate with their irregular ramifications far into the cartilaginous layer—as far, indeed, as the outermost limit of the zone of proliferation—without being surrounded, as they usually are, by calcification and ossification. Thus a rickety epiphysis is made up of cartilage irregularly interspersed with ossified and calcified patches, and with medullary spaces, the latter being surrounded, now with cartilaginous, now with already ossified tissue.

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[1] Comptes Rendus, 1873, LXXVII. p. 1105.

While, as I have already stated, opinions differ concerning the phenomena of normal ossification, and especially as to the ultimate destiny of the cartilage-cells, there can be no question that, in rickets, some part at least of the cartilage-cells undergoes direct conversion into bone-corpuscles (Strelzoff's metaplastic type of ossification). Others are transformed, according to Klebs, when the capsules containing them are opened up, into medullary cells (osteoblasts), which ultimately develop, as the disease advances, into connective-tissue corpuscles. In this way the vessels in the medullary spaces come to be sheathed in a layer of fibrous connective tissue of unusual thickness.

Phenomena similar to those taking place in the cartilage occur likewise in the periosteum. This, too, becomes several millimetres thick and extremely vascular ; it is often impossible to detach it from the bone without stripping off large bits of porous bone tissue along with it. As seen in transverse sections through the entire bone, it forms a broad zone of reticulated and blood-stained aspect around the compact tissue of the cortex. Microscopical examination demonstrates its corpuscular elements, at some distance from the surface, undergoing very active proliferation ; they may be observed to pass gradually into bone-corpuscles. The direct transformation of the connective-tissue corpuscles of the periosteum into bone-corpuscles (Virchow) can only be demonstrated in rickety bones ; and this (metaplastic) type of ossification, both from the periosteum and the cartilage of the epiphyses, is allowed to occur in them even by those who, like Strelzoff, believe the bone-corpuscles to originate, normally, in quite a different way. Strelzoff is inclined to think, however, that some only of the connective-tissue corpuscles are converted into bone-corpuscles, the remainder blending with the intercellular substance, which grows more and more dense. Here, as in the epiphyses, the deposit of calcareous salts in the proliferated layers is but scanty ; hence, in transverse sections, we see layers of compact, well ossified cortical substance alternating with concentric strata of unossified trabeculæ forming a network; the latter are made up of a fibrous matrix with connective-tissue or bone-corpuscles embedded in it, and including large, highly congested medullary spaces.

The irregularity of the periosteal bone-growth is well seen in the flat bones—the scapulæ, the pelvic, and especially the cranial bones. When cut across, they present a highly congested, coarsely reticulated, pumice-like tissue, deposited just under the periosteum, especially at their edges; while their central parts, and especially their tuberosities, are attacked at a later period, and less severely. Thus we get irregular surface thickenings and marginal protuberances; elsewhere, owing to the process of ossification lagging behind that of absorption, we get thinning and even complete disappearance of the bone-tissue. (Cf. Craniotabes.)

Rickety bones differ from those that are normal no less in chemical composition than in structure. The numerous and careful comparative analyses of bones in various stages of development made by Friedleben have not only confirmed the statements of previous inquirers as to the diminution of earthy matter, but have also led to the discovery of other important alterations. Friedleben ascertained: 1. That the proportion of earthy salts is greatly reduced at the height of the disease, and chiefly so in the newly formed tissue. 2. That the bones become specifically lighter. 3. That the unossified cartilage contains an increased proportion of water. 4. That the amount of carbonic acid is slightly increased. 5. That the long bones contain a larger proportion of fatty matter.

The long bones of healthy children, after they are dried, have been found to consist, on an average, of 63–65 per cent. of earthy salts, and 37–35 per cent. of organic matter. The following tables illustrate the composition of the bones in rickets.

(The figures in parentheses refer to cases that were convalescent, or in which the disease had run its course.)

	Marchand.	Davy.[1]	v. Bibra.	Ragsky.[2]	Ephraim.	Lehmann.	Boettger.[3]	Friedleben.	Schlossberger.
Femur..........	20.60 *inorgan.* 79.40 *organ.*	(37.80 62.20)	....	....	35.73 64.27	....	20.89 *inorgan.* 79.11 *organ.*	52.85 *inorganic.* 47.15 *organic.*	....
Tibia..........	....	26.00 74.00	....	....	....	39.32[4] 60.68	24.70 75.30	48.37[5] (39.65 51.63 60.35)	....
Radius	21.24 78.76	....	....	....	....	....	20.00 80.00	....	....
Ulna..........	....	....	(58.30 41.70)	....	....	....	....	....	....
Ribs..........	....	....	....	....	....	....	25.65 74.35	37.19[6] 62.91	....
Humerus and Scapula..........	....	....	....	18.88 81.12	....	....	....	....	....
Sternum..........	29.36 70.64	....	....	....	....	....	....	....	....
Vertebræ..........	18.68 81.32	....	....	....	....	....	....	32.29[5] 67.71	....
Skull (occipital and parietal bones)...	....	27.10 72.90	....	....	....	....	....	51.06[7] 48.94	52.87[8] 47.13

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[1] In *Friedleben*, loc. cit. p. 148.

[2] *Rokitansky*, Pathol. Anat. 1. Auflage. II. 201.

[3] In *Stiebel*, p. 537.

[4] Mean of three analyses.

[5] Mean of two analyses.

[6] Mean of seven analyses.

[7] Mean of eighteen analyses.

[8] Mean of five analyses.

When recovery sets in, an abundant precipitation of lime and rapid ossification take place in the newly-formed layers of tissue. The epiphyses and the sub-periosteal deposits lose their spongy, reticulated aspect, and become very dense and hard. The bone as a whole grows very heavy (rachitic sclerosis or eburneation). As a result of this process, hard, nodular periostoses are often left upon the flat bones, especially on the occipital, more rarely on the parietal and frontal (Taylor).

The process of repair follows much the same course in the willow-stick, and in the far less common complete fractures of the bones. The greater frequency of the former must be attributed, as Virchow has pointed out, to the resistance offered by the thickened periosteum and the soft outer layers of bone to complete fracture. Hence the bone is usually broken on one side only; and even on that side only the innermost brittle lamellæ are usually fractured. The bone is bent towards the side of the fracture by mechanical pressure and muscular action, and the medullary cavity more or less narrowed accordingly. The callus, which is principally thrown out on the fractured, concave aspect of the bone, causes a marked thickening of the cortex during the process of repair. In this way, the medullary cavity may be wholly, or all but wholly blocked, while the angle formed by the two parts of the bone is, to a large extent, obliterated.

We know scarcely anything about the composition of the urine in rickets, beyond the isolated statements of Marchand, Ephraim, and Lehmann, concerning an increase in the proportion of phosphate of lime and the presence of lactic acid, to which I have already had occasion to allude. An increased elimination of uric acid (up to .18 per cent.) was observed by Ephraim alone.

The rickety changes in the bone-tissue are not, *per se*, fatal. In examining the body of a rickety child after death we almost always find, besides the changes in the bones, some organic lesion of the viscera to account for death. Apart from intercurrent disorders, which stand in no sort of causal relation to rickets, we commonly find evidence of chronic disease in the digestive apparatus—traces of protracted catarrh of the bowels, swollen mesenteric glands, enlargement of the liver (fatty infiltration), and overgrowth of the spleen. In such cases the body is usually emaciated, owing to the prolonged disturbance of nutrition; the muscles are flabby and shrunken, and the viscera in general anæmic. Next in order of frequency among the causes of death stand affections of the respiratory organs; we often find tuberculosis of the lungs or extensive catarrh with lobular collapse and broncho-pneumonia, less frequently croupous pneumonia or pleurisy. Sometimes, when death has been preceded by convulsions, we find the brain and its membranes congested and œdematous. Finally, in rare instances, as when death has been caused by spasm of the glottis, we may find no signs of fatal mischief on post-mortem examination.

Analysis of Individual Symptoms.

Deformities of the Skeleton.

Speaking generally, there are two ways in which they may be produced. First, as an immediate result of the enlargement of the bones by the proliferative processes already described, which is more noticeable during life in the epiphyses than in the diaphyses, because the former are less thickly covered by soft parts, and therefore more accessible to inspection and palpation. Secondly, deformity may result from the abnormal softness of the bones, due to the structural and chemical changes that take place in their tissue, and render them less capable of resistance to the mechanical forces brought to bear upon them. Strelzoff has discovered an additional reason for the impaired resisting power of rickety bones. He finds that in them the disposition of the osseous trabeculæ is an abnormal one. Instead of being arranged concentrically in the long bones, as they ought to be, they are more radially disposed, and this arrangement is not so well suited to withstand the forces acting on the bone. It would be interesting to study the process of repair in rickety bones, with especial reference to this point.

The following are the principal forces that act upon the bones: the weight of the body, muscular contraction, atmospheric pressure, and the pressure exerted by the growth of an organ enclosed in a bony case. I will now describe the alterations taking place in different parts of the skeleton individually.

The alterations in the skull depend principally on the age at which the disease makes its first appearance. They are most marked when it begins—as it generally does—before the closure of the sutures and fontanelles, *i. e.*, during or very soon after the first year of life. In typical cases the head appears unusually large, but its circumference, as proved by the measurements of Ritter v. Rittershain, is not really any greater than in healthy children of the same age; its apparent bulkiness is due to its being out of proportion to the face and the rest of the skeleton, whose growth is delayed. Shaw gives the proportion between the cranium and face in rickety children as $7\frac{1}{13} : 1$, while in healthy children it only amounts to 6 : 1. The frontal and occipital bones, with the parietal eminences, are very prominent, and the skull thus acquires a distinctly square shape. The anterior fontanelle, instead of gradually closing at about the fourteenth or fifteenth month, remains open or may even be enlarged by the expansion of the growing brain. It may continue open till the third year or even longer, its compressibility varying from time to time in accordance with the fulness of the ventricles and cerebral blood-vessels. Its shape is often altered; instead of its usual four-cornered, or even square outline, it presents an irregular margin studded with little projections. The sagittal, frontal, and coronal sutures may be traced to a variable distance from the anterior fontanelle. Together with the lambdoid suture, their margins are soft and gaping; they appear thickened and pliable. The posterior and the smaller lateral fontanelles may also remain patent for a long time.

The occipital bone presents the striking phenomenon described by Elsaesser under the name of "craniotabes;" its expanded portion is thinned in patches, which yield to the finger like parchment. It is true that even in children who are not rickety the occipital bone, particularly at its edges, is often soft and pliant; but it only presents these characters during the first few months of life. During the latter half of the first year, at the time when rickets is most common, the occiput of healthy children is usually quite firm and refuses to yield to the finger. At this period, accordingly, the signs of craniotabes are very characteristic. The thinning of the occipital bone is brought about by the contending pressure of the pillow from without and the brain from within, when the infant is lying on its back. Friedleben has pointed out an additional cause, viz., that the absorption of newly-formed layers of bone, which is far from being uniform even under normal circumstances, is still more unequal in rickets; hence, it leads to greater and more striking differences in the thickness of the bones in this disease than in health.

After recovery the sutures and the anterior fontanelle are often found to be depressed below the level of the bones around them. This is owing to the undue prominence of the deposits along the edges of the cranial bones, a prominence which they maintain during their subsequent ossification; the sutures thus come to resemble shallow grooves with raised edges. This condition is often particularly well marked in the sagittal suture.

The systolic murmur audible over the fontanelle, discovered by Fisher, of Boston, in 1833, and adopted by well-known physicians as an important diagnostic sign of rickets, proves nothing more than that an unossified membrane is better fitted than the cranial bones to transmit the sounds generated in the cerebral vessels (probably in the arteries at the base of the brain) to the ear or stethoscope. Inasmuch as the fontanelle is usually of abnormal size in rickety children, and remains open for a long time, we can readily understand that it should appear to be specially associated with the disease in question.

As regards the facial bones, it is the defective development of the jaws that strikes us most; moreover, it exerts an important influence on the progress of dentition. According as the onset of the disease is early or late, the first appearance of the teeth may be delayed, or the intervals at which the individual teeth cut the gum may be unduly protracted. Should the child become affected before a single tooth has come through, teething is altogether arrested till the twelfth or fifteenth month, or even later. On the other hand, should the child already possess a few teeth before it is attacked by rickets, the next batch emerge, not after a few weeks' interval, but after an interval of months; and even then dentition does not resume its proper order until the disease has run its entire course. This delay and irregularity in the appearance of the teeth forms one of the earliest and most constant symptoms of rickets in young infants, and is therefore of great diagnostic value. I have already mentioned that the teeth are of bad quality and are soon shed.

The deformity of the thorax is principally due (if we put aside the "rickety rosary") to atmospheric pressure. The softened ribs yield to the suction which the lungs exert on the parts around them, and especially on the thoracic walls; they are drawn inward, just as the intercostal spaces are normally drawn in; the sides of the chest, where its walls are least able to resist pressure, are the first to yield. The atmospheric pressure is increased by the abdominal distention which is usually present, and by the bronchial catarrh; for these conditions hinder the entrance of air into the lungs, and thus interfere with the equalization of the external and internal pressure during inspiration. The ribs may thus come to be bent inward or even partially fractured, and the thorax presents a broad, shallow groove extending on either side from the arm-pits to the hypochondria. Posteriorly, on either side of the vertebral column, the ribs form projecting arches which pass into the lateral region of the chest—towards the axillæ—not by a gentle curve, as they normally do, but at a sudden angle. Further, the sternum is thrown forward like that of a bird (*pectus carinatum*). The clavicles follow it; they no longer lie in the anterior plane of the body, but pass backward to the receding shoulders; sometimes, too, they are bent at an angle or even broken. The scapulæ are not usually much altered. On careful examination, however, they are sometimes found thickened at their edges.

The absence of those forces which are brought into play by respiration explains how it is that the peculiar deformity of the thorax (as pointed out by Ritter von Rittershain) is not met with in fœtal rickets, while other distortions and deformities take its place. Many authors attribute the lateral depression of the chest-walls to the mechanical pressure exerted in lifting children by putting the hands under their arm-pits; but this would hardly account for the symmetry of the depressions, especially in the lower part of the chest, though it may undoubtedly be the cause of occasional willow-stick fracture in particular ribs.

The deformities of the thorax cause displacement of the thoracic viscera, often increased by the curvature of the vertebral column. The lateral compression of the chest brings the heart, more particularly, into contact with a larger area of the chest-wall. Its impulse may thus appear to be unusually diffused.

When the disease ends in recovery, the swellings on the ends of the ribs subside, or are obliterated by the progressive growth of neighboring parts; but the deformity caused by the lateral inflexion of the ribs is permanent, and remains throughout life to bear witness to an attack of rickets during infancy.

Curvatures of the spine are rendered possible by the abnormal softness of the intervertebral cartilages and of the bodies of the vertebræ themselves, together with their irregular growth and unequal development; further, by the flaccid condition of the muscles and the presence of thoracic deformity. Kyphosis in the lower dorsal region is most common. This is due to the weight of the trunk when the child sits bending forward, the forward tendency not being adequately counteracted by the extensor muscles of the back, which are either imperfectly developed or fatigued. When this form of curvature first shows itself, it may be rectified by simply raising the trunk of the body; but at a later period, when the shape of the vertebræ and intervertebral disks has been altered by continued pressure, and they come to resemble wedges with their narrow end forward, it can no longer be effaced by such simple measures. Should the thorax be much compressed from side to side, the upper dorsal region of the spine is bent with its convexity outward. Then, too, the cervical region as a rule, the lumbar region occasionally, present a marked degree of lordosis. The antero-posterior curvature is commonly associated with a slighter degree of lateral curvature. Curvature of an extreme kind is rare in rickets. When present, it must be ascribed partly to feebleness of the muscular system and the persistent maintenance of a faulty attitude (as when the child is always dandled on the same arm), partly to deformity of the pelvis or the lower limbs, for in the latter event equilibrium in sitting or walking can only be maintained by bending the spine sideways, so as to compensate for the unequal development of the limbs (according to Bouvier, the convexity of the curve is always directed towards the longer limb).

The bones of the pelvis participate in various ways in the deformity. The degree and manner in which they do this depend partly on the age at which the disease sets in, partly on the existence and degree of other deformities. Accordingly, the deviations from the normal standard of pelvic symmetry are various. We do not always find the peculiar form that used formerly to be described as, *par excellence*, the "rickety" pelvis (a pelvis narrowed in its antero-posterior diameter, obliquely elliptic, reniform, cordate, etc.). Many of the peculiarities of the rickety pelvis may be observed, as Kehrer points out, even in the fœtus, and in infants who have not yet learned to walk; so that they must be set down to muscular contraction (ileopsoas, erector spinæ, glutæus medius, etc.). There are other causes, too, which tend to increase the variety of pelvic distortions in rickets: the bones of which the pelvic girdle is made up, and the individual elements of those bones, may be affected in very various degrees by the process of softening; previous deformities of the trunk or lower extremities may influence the pelvis; finally, the nature of the pelvic distortion will be influenced by the usual attitude of the child when it becomes affected by rickets—whether lying down, carried in the arms, or able to walk.

None of these pelvic deformities cause trouble in childhood. Their importance does not become apparent, save in the female sex, as a possible hindrance to parturition. The reader may consult works on obstetrics for a description of the individual varieties of rickety pelvis.

The first sign of rickets in the bones of the extremities is a thickening and expansion of the epiphyses. This is principally due to proliferation of the cartilage elements. It is sometimes assisted by the pressure of superincumbent parts, which flatten them and make them bulge in all directions. The articular ends of the bones may subsequently become displaced or twisted to one side. This is most often the case with the femur, both at its upper and at its lower end. In consequence of this change, the ligaments become relaxed on one side, and shrink on the other, the joint assuming an oblique position (genu valgum, varum).

When a child is attacked by rickets before it is able to stand, the bones of the extremities obey the influence of the strongest muscles attached to them. Accordingly, in very young children the deformity produced is a mere exaggeration of the natural curvature of each bone. The leg is bent forward and outward, the fore-arm towards its flexor aspect. Even if the child has learned to walk, the weight of the body usually bends the legs in the same direction, but in a greater degree. We often find them bent abruptly inward, especially at their lower third. The deformity may be so extreme as to bring one foot over, or even across, the other. Less commonly the legs are bent the opposite way, with the concavity outward, in the form of the letter X. This variety seems chiefly to occur when the lower end of the femur has been turned inward (*genu valgum*); perhaps, too, special circumstances, such as a habit of crawling on the knees, may contribute to produce it. A curvature of the leg with its convexity forward is somewhat more common; and various forms of incomplete fracture may modify the resulting deformity in the strangest ways. It is to such incomplete fractures, moreover, that the graver deformities of other bones are due—*e. g.*, those met with in the upper arms or fore-arms of children who support themselves on their upper extremities; also those occurring in the thigh-bones. The latter are usually bent abruptly, with their convexity outward. The upper arm, on the other hand, has its convexity directed inward, and, the fore-arm being bent the opposite way, the upper extremity, as a whole, comes to present a zig-zag outline. When the upper arms are greatly distorted in consequence of partial fracture, we always find (to judge from my own experience) similar incomplete fractures of the clavicles; but the converse does not hold good; the clavicle may be broken without fracture of the humerus.

As regards the comparative frequency of the different kinds of deformity, and the order in which they are usually developed, Guérin ventures on a generalization. He believes that the lower epiphyses of the bones of the leg are always the first to be affected, the disease then extending upward. This is true only of those cases in which rickets comes on almost imperceptibly, in children upwards of a year old, whose cranial bones are already consolidated. It is not true of that far larger group of cases in which the disease sets in about the time of the first dentition. Hence, the skull is the first part of the skeleton that suffers; its fontanelles and sutures remain open, or may even increase in size; the appearance of the teeth is checked. It is not till later that the ends of the ribs and the epiphyses of the long bones begin to swell; this change showing itself first either in the hands or in the feet, and spreading from thence to the other joints. The vertebral column does not appear to be affected till a relatively late stage in the course of the disease. I know of no data concerning the exact period at which the pelvic bones may become involved; they are not very accessible to examination during life, and post-mortem examinations usually display a manifold variety of deformities at once.

As regards general increase of stature, Shaw affirms that this is checked far more in the lower than in the upper half of the body; the former being about one-third, the latter only one-thirteenth, less than it ought to be. Ritter von Rittershain found that of forty-two rickety children, one only attained the normal average stature of a healthy child at the same age; all the rest fell short of it by 3–6 centimetres, or even more. It is not until the disease has entirely spent itself that the growth of the body in length is actively resumed; but this resumption of activity is often insufficient to make up for the effects of the previous delay. Hence, rickety subjects are often stunted for life, even though they may have escaped any of the more serious deformities of the limbs or spine.

Disorders of the Digestive Apparatus.

In my general description of the disease I pointed out that the changes in the bones were preceded, in the vast majority of cases, by disturbances of digestion. The latter usually persist, more or less severely, throughout the whole course of the malady. The enlargement of the abdomen, which is associated with the catarrh of the alimentary canal, is particularly striking; in rare instances—usually in children much reduced by chronic diarrhœa, and on the point of dying from exhaustion—we find the belly flat or retracted. In such cases, the swollen mesenteric glands may often be felt through the abdominal walls during life; in the vast majority, however, this is impossible, owing to the tympanitic condition of the bowels.

Many writers on rickets affirm that the liver is usually, or at any rate, frequently enlarged and fatty. Observations on the living subject are not of much value as evidence on this point; there are many difficulties in the way of a thorough examination of the liver, and erroneous conclusions as to its true size may easily be arrived at. The meteorism which is so commonly present is enough to make any accurate determination of the hepatic outlines by percussion and palpation impossible; for the liver is pushed upward and backward, besides being twisted on its horizontal axis. In this way, we may be led to believe that the liver is smaller than it really is. On the other hand, serious narrowing of the chest may cause downward displacement of the organ, and a delusive semblance of enlargement. But even if we set aside the difficulties in the way of physical examination, we have to bear in mind that in young children, especially when at the breast, a certain degree of fatty liver is normal; and that the organ may thus exhibit—apart from any disease—a volume relatively greater than in the adult. Lastly, the disturbances of the respiratory function that are so very common in rickety children, and the venous stagnation to which they give rise, may cause enlargement of the liver from passive congestion. Accordingly, we are justified in concluding that clinical observation furnishes no certain proof that the liver is *abnormally* infiltrated with fatty matter in rickets. Post-mortem inspection, again, discloses a considerable degree of hepatic enlargement in a small minority of cases only; and here I may observe that the death of rickety children often occurs under circumstances of extreme emaciation due to disordered nutrition; and that fatty liver, in such cases, even when it exists, does not stand in any special relation to rickets, but possesses the same significance as in all other forms of wasting disease.

The case of the spleen is altogether different. Splenic enlargement may be demonstrated in a large proportion of rickety children by percussion, and still more certainly, by palpation.

The rounded anterior edge of the organ may often be felt under the costal margin, or even well in front of it, over a considerable area, so that, in spite of the meteorism, we may conclude that the spleen is positively enlarged. Ritter v. Rittershain found a marked degree of splenic enlargement in ten out of thirty-five post-mortem examinations. When rickets is superadded to some chronic constitutional disorder (*e. g.*, when it comes on after recovery from inherited syphilis), or when it is due to hereditary predisposition, enlargement of the spleen seems to be one of its earliest symptoms. The enlargement is usually due to corpuscular overgrowth, as in other diseases connected with a dyscrasia. Amyloid degeneration of the spleen is probably rare, and may be traced to extensive follicular ulceration of the intestines, to tuberculosis, etc.

Complications.

Bronchial catarrh is the most frequent complication of rickets. The rickety child is specially liable to this disorder, owing to its being badly nourished and less able to resist cold. In consequence of the reduced capacity of the deformed thorax, even a slight catarrh, such as would give little trouble to a healthy child, may cause severe dyspnœa and cyanosis. Further, the weak state of the respiratory muscles readily allows complete blocking of individual bronchi to occur, with collapse of the corresponding parts of the lung tissue.

Broncho-pneumonia and pulmonary tuberculosis are also not unfrequently associated with rickets. Spasm of the glottis is specially worthy of notice, as it is extremely common in rickety children. Elsaesser and others have sought to connect it with craniotabes, ascribing the spasm to pressure on the brain through the softened occiput. But the laryngeal spasm is often observed without there being any marked softening of the occipital bone; indeed, it is a far more frequent complication of rickets than craniotabes itself. Scrofulosis is very commonly found in association with rickets. Cerebral complications (internal and external hydrocephalus, meningitis) are less frequent.

Diagnosis.

It is very easy to recognize fully developed rickets from the description given above. We only know of one other disease capable of producing morbid changes in the bones of an infant—especially swelling of the epiphyses—similar to those produced by rickets; I allude to hereditary syphilis (*Vide supra*, p. 173). But syphilis is nearly always observed during the first few days or weeks of life, at a time when rickets is excessively rare, even if we are indisposed to believe that the recorded examples of very early rickets may have been really due to syphilis. Moreover, syphilitic children, when born alive, usually though not invariably (Waldeyer, Koebner) show other signs of inherited taint; or our doubts may be set at rest by inquiring into the history of the parents, a precaution that ought never to be omitted in such cases. Again, the syphilitic disease of the bones often terminates in suppuration and complete detachment of the epiphyses; also in the growth of osteophytes; changes not met with in rickets (cf. Birch-Hirschfeld, in Archiv der Heilkunde, XVI. 1875, p. 166).

Local deformities of the skeleton, such as spinal curvature or hydrocephalic enlargement of the skull, may be distinguished from rickets by the very fact that they *are* local, and unattended by beading of the ribs or swelling of the epiphyses of the long bones. Our doubts may be set at rest by the discovery of the cause in each particular instance, as caries of the vertebræ, hemiplegic paralysis and atrophy of muscles, absorption of pleuritic effusions, etc.

It is a more difficult matter—though one of great importance as regards treatment—to recognize the first beginnings of the disease. The disorders of digestion which usually precede the changes in the bones, especially in younger children, are not in themselves characteristic of rickets; but when they occur during the second half-year of life, about the time of the first dentition, and show an obstinate tendency to recur, they ought to make us suspect the approach of rickets, whose earliest *specific* signs will be furnished by the delay and irregularity in teething, the behavior of the sutures and fontanelles, and the local sweating of the head.

Whether the state of the urine—more especially the presence in it of lactic acid, or an excess of earthy salts—may not furnish diagnostic signs even earlier than the skeleton, must be decided by future inquiry.

Course, Duration, and Issues.

Apart from those rare cases of "acute" rickets (p. 183), which run their course in a few weeks, the disease always lasts for months or even years. The earlier the age at which it sets in, the more rapid and severe are the changes wrought in the bones, and the associated troubles—especially those of the respiratory organs,—and the more profound, accordingly, the interference with the child's general health and nutrition. That form of rickets which begins during the second year or even later, runs a more sluggish course; it is not attended by fever or any considerable degree of constitutional disturbance. Its course is often interrupted by pauses of variable length, during which the bones cease to swell, the digestive troubles subside, and nutrition improves in consequence; the resumption of morbid action being generally ushered in by an exacerbation of the digestive disorder, by restlessness and fever.

Those cases of rickets that begin late and run a slow course almost always end favorably. There remain a certain plumpness of the affected bones, more or less deformity, and permanent stunting of the body. When the disease sets in early, *i. e.*, during the first twelve months, it may also terminate in recovery; this usually sets in with an improvement in the child's nutrition and general state; the teeth come through more quickly, the swollen epiphyses subside, and the bones become consolidated. But many of the younger sufferers never live to reach this stage; they are destroyed by one or other of the complications enumerated above, especially by disorders of the respiratory apparatus. Since the latter are most prevalent during the cold season, this is the most dangerous time of year for rickety subjects. In summer, again, they are liable to gastro-intestinal catarrh, which claims its share of victims from among them.

Prognosis.

Although the changes in the bones are not in themselves fatal, the prognosis of rickets, as regards life, is not unconditionally hopeful: it depends chiefly on the intensity of the nutritive disturbance and the complications. These, as I have already pointed out, are most severe in younger children; hence, the prognosis is more favorable in proportion to the patient's age. Of course it also depends on the child's constitutional vigor, and the amount of care and skill bestowed upon it, etc.

The deformities of the skeleton, when they are slight in degree, may entirely disappear. Of those that are permanent, two only may prove troublesome in after-life—chicken breast in both sexes, and pelvic distortion in the female. The possible risk to which a woman with a distorted pelvis exposes herself by marriage, should always be impressed on the mind of her relations.

Treatment.

Both in the prevention and the actual treatment of rickets, the chief business of the physician is to lay down hygienic rules. Prevention must be held in view when previous children of the same family have suffered from rickets, or when the parents show traces of having had the disease in early life, or are in weak health, or affected by any disease, which, like tuberculosis, favors the development of rickets in their offspring. When syphilis exists, it must of course be energetically attacked.

The feeding of the infant is the main thing to be attended to. We know that improper feeding stands foremost among the causes of those gastro-intestinal disorders which are so dangerous to infant life; and, in speaking of the etiology of rickets, I pointed out the intimate connection between those disorders and the malady in question. During the first few months after birth, these disorders may be prevented by keeping the infant at the breast; should the mother be unable to suckle her own child, a good wet-nurse should be provided. The milk of mother or of nurse, provided that they are well nourished, is quite sufficient till the infant is six or seven months old—till the first teeth come through. From this time forward the mother's milk should be supplemented by some digestible food, such as broth with the addition of isinglass, meat-shavings, and other substances which I shall presently enumerate. Lastly, the infant should be weaned when it is ten or twelve months old. I need hardly add that the circumstances peculiar to each case ought to be considered in fixing the right time for weaning, whether partial or complete; among those circumstances, the child's own condition and the state of its digestive organs, stand foremost.

Not one among the many artificial foods recommended for infants can be regarded as an effectual substitute for good human milk. The close similarity of composition between the milk of the lower animals and that of man will always insure its preeminence among substitutes for the latter. Cow's milk is generally chosen, because it is easily got: it must be sweetened with lactose, and diluted to suit the age of the infant. I do not know whether the milk of the ass and mare, which approximate most closely in their composition to human milk, have been shown to be practically superior to cow's milk. Next to the latter, I recommended Nestle's infant food, from personal experience of its value and convenience. During the earlier months of life, infants often do very well on the condensed milk manufactured at Cham, in Switzerland, Kempten, in Bavaria, and other places. But if any of these articles be employed exclusively for any length of time, the infant accumulates too much fat, while, at the same time, it is less vigorous and less able to resist disease. This may possibly be due to the disproportionate amount of carbohydrates (sugar, dextrin, starch), as compared with that of the albuminates, in condensed milk. I am therefore in the habit of ordering light broth in addition, from an early age. When cow's milk proves indigestible, the yolk of an egg beaten up with water, sugar of milk, and a trace of salt, forms a good substitute. On other kinds of artificial food my own experience does not entitle me to pronounce an opinion. Beneke[1] affirms that finely-powdered lentil-meal (prepared by W. I. van Coppenaal in Amsterdam, by Hartenstein at Niederwiesa in Saxony)—the main ingredient in the universal panacea known as Revalenta Arabica (Revalescière)—deserves to be more largely employed than it is. Biedert[2] recommends a cream mixture. Other preparations, such as Liebig's soup, Loeflund's food for infants, boiled arrowroot, etc., need not be entirely proscribed, although they are certainly less useful in practice than those given above. It is sometimes necessary to have a great variety of substitutes for human milk at one's disposal, as we never know beforehand which of them will suit a particular child, and also because, when digestion is upset, or the child does not seem to thrive as well as it ought, we may find it necessary to vary its diet frequently. It sometimes happens that an infant will do well on one of the less popular foods after all the more famous ones have been tried in vain.

Whatever food be chosen, the utmost care must be taken in preparing it, in keeping it, in scrupulously cleansing the infant's mouth; indeed, these precautions are indispensable even in the case of healthy children.[3]

Warm or tepid baths, serviceable for healthy children, are yet more so in the treatment of rickets. Sea-salt, or the mother-liquor of any of the brine-springs, or aromatic herbs, or a decoction of malt, may be added to the bath with advantage. It is only when the thorax is much deformed and the resulting dyspnœa severe that we are compelled to eschew baths for fear of increasing the dyspnœa. In such cases we may desire the body to be frequently sponged with warm brine, and the limbs rubbed with spirit and aromatic liniments. When there is much sweating about the head, the latter may be bathed with cold water.

Pure, dry air is essential; the child should be kept out of doors as much as possible and exposed to the sun. It should be shielded against the risk of taking cold by warm clothing, and especially by the immediate change of linen, etc., wetted by its evacuations.

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[1] Berlin. klinische Wochenschrift, 1872, No. 15.

[2] Virchow's Archives, LX., p. 352.

[3] For an excellent and detailed account of the whole matter I willingly refer the reader to *Kehrer's* lecture on the Feeding of Infants (Volkmann's collection of Clinical Lectures, No. 70).

To prevent the occurrence of deformities, or to mitigate their severity, it is important to make the child lie, not on soft feather beds, but on a hard mattress stuffed with horse-hair or dried seaweed; its head should rest on an annular cushion into whose central opening the occiput may fit. The utmost care should be taken to avoid the risk of willow-stick fracture of the bones in grasping and lifting the child. The attendants should be warned against helping the child to stand or walk, or carrying it much in their arms. When not asleep the child ought to lie or sit on a blanket spread on the floor, or, when the weather is fine, in the open air, out of reach of anything by laying hold of which it may raise itself up.

As regards strictly medicinal treatment, I may begin by saying that of the multitude of remedies formerly employed in rickets, whose popularity was founded either on mere experience or on theories devoid of any scientific basis, only a few remain in use. We are obliged to use drugs in the treatment of the digestive disorders incidental to rickets, when our dietetic measures have failed. We prescribe one or other of the remedies usually employed in the dyspepsia or gastro-intestinal catarrh of children, according as the leading symptom is anorexia, vomiting, diarrhœa, acidity, or distention of the abdomen. The individual remedies are more fully described in the articles on Diseases of the Digestive Apparatus. Lime, in virtue of its alkaline and astringent properties, meets most of the indications at once; and this alone is a sufficient reason for giving it in rickets, though not, of course, to the exclusion of other remedies. Moreover, the demonstrated poverty of rickety bones in lime and the important part played by lessened supply of lime in the artificial production of rickets (p. 176), would lead us to anticipate some benefit from the free administration of this substance; and it is not known to have any undesirable effects. We may, therefore, safely give lime throughout the entire course of the disease. The officinal lime-water (*liquor calcis*) is the most convenient preparation; it may be given several times a day, in doses varying from a teaspoonful to half an ounce, or else mixed with the liquid food, particularly the cow's milk (whose normal reaction is faintly acid), or even with broth, etc. Carbonate of lime is less suitable, especially if there be a tendency to tympanitic distention of the bowels, on account of its liberating carbonic acid in the stomach. The same objection applies to the powdered oyster-shells (*testa preparata*) that people are so fond of giving; there is a further drawback to their use: the angular particles may irritate the bowel mechanically (Schlossberger).

Further, we must endeavor by means of remedies to assist the diet and regimen in improving the state of the infant's nutrition. Tonics are primarily indicated, save when our attention is claimed by some intercurrent disease, especially of the respiratory organs. The more digestible preparations of iron, such as the salts of iron with the organic acids, should be prescribed in combination with aromatic bitters, such as the compound tincture of cinchona or gentian. Should a more powerful astringent be desired, the tincture of the chloride of iron may be given. When the digestive system is in good order the moderate use of artificial or natural chalybeate waters, either alone or mixed with milk, is highly to be recommended. My own experience entitles me to say that the water of the Weinbrunnen, at Schwalbach, and waters holding pyrophosphate of iron in solution, are well borne, even by children with feeble digestive powers. All the fashionable chalybeate springs are well adapted for a summer course of baths and beverages; I may mention, as specially appropriate, the waters of Driburg, which are rich in iron and lime; those of the Renchthal, in Baden; those of Petersthal (and also of Freiersbach), which are remarkably easy of digestion.

Cod-liver oil, formerly regarded almost in the light of a specific both for rickets and scrofulosis, can only be administered when the digestive organs are in good order; it ought not to be given in hot weather, when it is very apt to disagree. During the colder months, on the other hand, in doses gradually increased from a teaspoonful to one—at the most two tablespoonfuls daily, it is willingly taken by rickety children, and usually with the best effect.

No special rules need be laid down for the treatment of the complications. I may, perhaps, repeat that in rickety subjects apparently slight affections of the respiratory organs, such as simple bronchitis, must be carefully watched; they are far more dangerous than when they occur in healthy children.

The deformities of the limbs that may be left after the disease has run its course require no special treatment, unless they happen to be extreme; for they tend to disappear of themselves as the child grows older. Malposition of the feet (*pes varus et valgus*) may be rectified by suitable apparatus (boots with steel splints on the outer or inner side of the ankle). When the lower limbs are much distorted, attempts may be made to straighten them by operation or by orthopædic appliances. For a detailed account of such appliances and of the management of spinal curvature, the reader may be referred to works on surgery.

LEEDS & WEST-RIDING
MEDICO-CHIRURGICAL SOCIETY

MALACOSTEON.

LITERATURE.—*Duvernay*. Traité des maladies des os. Paris, 1751, II. 321 seqq.—*Morand*, Histoire de la maladie singulière et de l'examen du cadavre d'une femme devenue en peu de temps toute contrefaite par un ramollissement général des os. Paris, 1752.—*The Same*, Mém. de l'Académie Royale des Sciences, 1753, p. 541, and Lettre a M. Leroy sur l'histoire de la femme Supiot. Paris, 1753.—*J. Pringle*, A remarkable case of fragility, flexibility, and dissolution of the bones. Philos. Transactions, 1753. XLVIII., p. 297.—*Navier*, Observations théor. et prat. sur l'amolissement des os. Paris, 1755.—*Van Swieten*, Comment. in Boerhaavii. aphorism, § 1261.—*Eckmann*, Dissert. descript. et casus oliquot osteomalaciae sistens. Upsalæ, 1788.—*Conradi*, Diss. de Osteomalacia. Götting., 1796.—*Metzger*, Diss. de Osteomal. Regiomont, 1797.—*Neumann*, Ueber Knochenweichung u. s. w. Abt. der Kais. Kön. Josephs-Acad. II. 173.—*Jo. Wallach*, Nonnullæ de osteomal. ejusque origine, etc. quæstiones. Dissert. Casselis, 1806, and Neue Zeitschrift f. Geburtsk. VI., Heft 2.—*H. F. Kilian*, Beiträge zu einer genauen Kenntniss der allg. Knochenerweichung der Frauen und ihres Einflusses auf das Becken. Bonn, 1829; and Das halisteretische Becken u. s. w. Bonn, 1857.—*Davis*, The Lancet, 1857, Febr.—*Lobstein*, Traité d'anatomie pathologique. Paris, 1833, II., 115, seqq.—*Rees*, Guy's Hosp. Reports, 1835, April.—*Prösch*, Comment. inaug. de osteomalacia adultorum. Heidelberg, 1835.—*Curling*, Medico-Chir. Transactions, XX., 1836.—*J. Sturm*, De osteomal adultorum. Diss. Herbipoli, 1841.—*Simon*, Med. Chemie. Berlin, 1842. II., 506.—*Rokitansky*, Pathol. anatomie. Wien, 1844, S. 195, seqq.—*A. H. Swaagman*, De osteom. universa fem. atque de pelvis figur. mutat., etc. Groning, 1843; and Nederl. Tydschr. 1854, Decbr.—*Jolly*, Med. Chir. Transactions, 1844, XXVII., 2.—*Dalrymple*, Dublin Quart. Journ., 1846.—*C. Schmidt*, Ann. der Chemie und Pharmacie, 1847, LXI., 329.—*Gerstner*, Archiv f. physiol. Heilk., 1847, VI., 142.—*J. Niederer*, Ueber die Osteom. eines Beckens nach den Puberstätsjahren einer Jungfrau. Diss. Bern., 1848.—*Macintyre*, Med. Chir. Transact., XXXIII., 1850, 211; and Edinb. Med. Surg. Journ., 1851.—*Stanski*, Recherches sur les maladies des os désignées sous le nom d'ostéom., etc. Paris, 1851.—*C. O. Weber*, Ossium mutat. osteomal. universa effect. Diss. Bonn, 1851; and Virchow's Archiv, XXXVIII., 1.—*Virchow*, l. c. s. Rachitis, Handb.

der Spec. Path. u. Ther., 1854, I., 321; and Cellularpathologie, IV., Aufl. S. 502 seqq.—*Beylard*, s. Rachitis.—*Chambers*, Med. Chir. Transactions, 1854, XXXVII., 19.—*Collineau*, Union Méd., 1861, No. 123.—*C. T. Litzmann*, Die Formen des Beckens insbes. des engen Weibl. u. s. w. nebst einem Anhang über die Osteom. Berlin, 1861.—*Drouineau* (*Schützenberger*), De l'ostéom. Thèse. Strassbourg, 1861.—*Breisky*, Prager Jahrshr., 1861, II.—*A. E. Durham*, Guy's Hosp. Rep., 1864, X., 348.—*Pagenstecher*, Monatsschrift f. Geburtsk, XIX., 111. 1862.—*Gusserow*, Ibidem, XX., 19.—*Winckel*, Sen., Ibidem, 1863, XXII., 57.—*Winckel*, Jun., Ibidem, 1864, XXIII., 81.—*B. G. Kleberg*, Schweiz. Zeitschr. f. Heilk., 1864., III., 310; and Lehrb. d. path. Histologie, 1873, 3. Aufl. 579.—*Volkmann*, l. c. (s. Rachitis) S. 342.—*Schieck*, ein Fall von Gummibecken u. s. w. Diss. Leipzig, 1865; and Monatsschr. f. Geburtsk. 1866, XXVII., 178.—*Schützenberger*, Gaz. Méd. de Strassbourg, 1867, No. 10.—*Drivon* (*Nérand*), Gaz. Méd. de Lyon, 1867, No. 22, 27, 28.—*H. Huppert*, Archiv der Heilkunde, VIII., 1867, S. 345.—*Jos. Jones*, New York Med. Record, 1869, March, p. 25.—*Nobiling* and *Buhl*, Bayer. ärtzl. Int.-Blatt, 1869, No. 39.—*Moers* and *Muck*, Deutsches Archiv für klin Med., 1869, V., 485.—*Stohmann*, Ueber Knochenbrüchigkeit erzeugendes Heu. In Virchow u. Hirsh's Jahresbericht, 1869, I., S. 551.—*Gusmann*, Osteom. bei einem Manne. Würtemb. Corresp.-Bl., 1870, No. 16.—*G. Calderini*, l'Osteomalacia. Memoria presentata, etc. Turin, 1870.—*Wegner*, l. c. s. Rachitis.—*Wilmart*, De l'osteomalacie, etc. Brüssel, 1871.—*G. Casati*, Sulla Osteomalacia osservata alla Maternita di Milano. Milan, 1871. Translated in Transactions of the London Med. Society, 1872.—*v. Weber-Ebenhof*, Die Osteomalacie mit besonderer Berücksichtigung des Gummi-Beckens. Prager Vierteljahrschrift, 1873, XXX.—*Heitzmann*, l. c. s. Rachitis.—*P. Bouley*, De l'ostéom. chez. l'homme et les animaux domestiques. Paris. 1874. Consult also the handbooks and journals of obstetrics and gynæcology and the literature of Rickets.

Historical Introduction.

Malacosteon (mollities ossium) is a chronic disease peculiar to adult life, which leads to a gradual withdrawal of earthy salts from all parts of the skeleton, and a consequent softening and abnormal pliancy of the bones, with ultimate deformity of the trunk and limbs.

Malacosteon differs essentially from rickets. The latter is a disease of the osteoplastic tissues, in consequence of which the newly-formed layers do not become properly ossified, and *remain* soft. The former is a disease of fully-formed bone, causing its tissue to melt and *become* soft.

It is not very long since malacosteon has been recognized as a distinct disease. True, cases of abnormal pliancy of the bones had been known for centuries; some of these cases, in which the deformity happened to be striking, had even become historical;[1] but they were at first regarded as mere curiosities, and then, after public attention had been drawn to rickets, as instances of the latter disease occurring in adults; rickets itself being termed, conversely, "infantile malacosteon." The first notice we find of a distinction between the softening of the bones in children and that in adults is in the work of Levacher de la Feutrie (1772); but his suggestion was allowed to drop, and the attention of physicians was almost exclusively directed to the difficulties in the way of parturition resulting from the pelvic deformity. Lobstein was the first who again insisted on the difference between the softening of the bones due to rickets and that due to malacosteon; moreover, he distinguished them both from that form of abnormal fragility or brittleness of the bones to which he gave the name of "osteopsathyrosis." The histological researches of the last twenty or thirty years have established the essential diversity of rickets and malacosteon; they have also separated other forms of atrophy of bone, *e. g.*, senile wasting and osteoporosis, which resemble the disease in question only in causing the bones to become brittle.

Morbid Anatomy and Chemistry.

The solidity of the bones is always impaired in malacosteon. When the disease is severe, they are pliant and soft, like india-rubber or cheese; they may be easily cut with a knife, and yield like egg-shells to the finger. They are always specifically lighter than healthy bones. Their size may be diminished uniformly, or they may exhibit alternate swelling and narrowing. When the periosteum, which often looks thickened and congested, is stripped off, the bone beneath it appears rough and studded with innumerable holes of various size, from which a liquid is seen to exude, this liquid being either bloody or yellowish, according to the stage reached by the disease.

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[1] Among these famous cases is that of the Arab Saadi, a contemporary of Muhammed, known as the "boneless man;" next, one recorded by Abou in the ninth century (Portal); then those of the Marquise d'Armagnac (Duverney) and Madame Supiot (Morand).

In the long bones we find the medullary cavity and the medullary spaces enlarged, the latter uniting to form channels of greater width. In the short and flat bones the cellular spaces of the diploë expand and coalesce to form larger cavities. The cortical layer is thinned, and its Haversian canals are dilated. It becomes coarsely cellular, like the diploë, and is ultimately reduced to a very thin lamella of compact tissue. In the more extreme forms of the disease even this lamella is no longer present, the bone resembling a piece of inflated and dried intestine. It consists of a large-meshed, spongy tissue, enclosing the proper medullary cavity, and held together by a thin coat of parchment-like tissue, continuous with the periosteum.

Microscopic examination shows that the bony trabeculæ that still remain are only in part made up of true bone-tissue, with well-formed corpuscles and calcified intercellular substance ; they partly consist of a soft tissue marked with concentric striæ, in which a doubtful remnant of a bone-corpuscle with indistinct processes may here and there be detected. This decalcified matrix presents exactly the same appearance, and behaves in exactly the same way to reagents and staining fluids, as the tissue left after the removal of the earthy salts from a normal bone by acids (the so-called "bone-cartilage") ; the morbid process has therefore been termed "halisteresis" (removal of salts) by Kilian. The decalcified tissue is chiefly met with close to the Haversian canals, which it completely surrounds. As we recede from the canals, we find it passing by imperceptible gradations into normal bone-tissue ; so that the interval between two canals is occupied by a band of unaltered bone-tissue of variable width, between two bands of the fibroid tissue described above. The bone-tissue is better preserved in proportion as it is farther from the medullary cavity. The process of degeneration or solution obviously progresses from the medullary cavity outward. It sets out from the Haversian canals, and gradually involves, first, the osseous trabeculæ of the cancellous tissue, then those of the cortical layer.

The medulla, while the morbid changes are actively going on, has an extremely congested appearance. The blood-vessels are widely dilated, and extravasations numerous. It may exhibit any shade of color, from light reddish yellow to deep purple, according to the amount of oily matter it contains. As the disease goes on, the medulla grows paler in hue; it assumes a yellow, honey-like or oily aspect. At a still later stage, when the disease has quite completed its course, we may find the medullary cavity occupied by a clear, viscid, mucoid or gelatinous liquid, either uniformly distributed or enclosed in cystic cavities.

On the ground of these differences in color, a distinction used formerly to be drawn between a red and a yellow form of malacosteon (*osteomalacia rubra et flava*); but we are now aware that the difference of tint indicates, not a difference in the form, but only in the stage of the disease. The changes which the medullary tissue goes through in malacosteon are generally analogous to those that normally occur with advancing years. Red marrow fills the bones in youth. It subsequently becomes fatty and yellow in patches (in the long bones), and in the very old it may even be gelatinous. Indeed, microscopical examination of the different varieties of marrow contained in the bones in malacosteon furnishes much the same results as that of normal marrow at different ages. The hyperæmic, dark red marrow contains, in addition to a multitude of extravasated blood-corpuscles, a number of cells with one, two, or several nuclei (embryonic cells), but only a few fat-cells, and these of small size. In the yellow medulla, on the other hand, the fat-cells predominate, or may even be exclusively present. They increase in size, and ultimately coalesce to form oil-globules of larger dimensions. Finally, they shrink and waste away, as the marrow passes from its yellow to its mucoid condition. There remains only a viscid, transparent matrix, containing a few scattered cells, and traversed by blood-vessels, and resembling the vitreous humor in its consistency (Virchow)—perhaps also allied to it in chemical composition. Hemorrhage is very prone to occur into this tissue from the residual blood-vessels. It may thus acquire a deceptive likeness to red marrow, but without becoming really identical with it.[1]

Chemical analysis of the affected bones invariably shows that the proportion of mineral salts (especially those of lime) is diminished, and that of organic matter correspondingly increased. The juice with which the bones are saturated has occasionally, but not always, been found to present an acid reaction; the difference in this respect between different observations being probably due to the varying quantity of blood contained in the bones, and perhaps also to the lapse of time between death and post-mortem inspection—an interval during which a supplemental formation of acid is undoubtedly capable of taking place. Lactic acid has repeatedly been demonstrated in the bones; also a striking augmentation of their oily constituents. The latter of these observations refers, in all likelihood, to that stage of the disease in which the marrow is yellow and fatty (*osteomalacia flava*). Finally, the organic basis of the bones, the ossein, seems also to undergo morbid change now and then, for C. Schmidt often failed to obtain any gelatin from bones affected by malacosteon.

The ratio of organic to inorganic matter (ash) is exhibited in the following table:

Analyses made by	Inorganic matter in 100 parts.	Organic matter in 100 parts.	Remarks.
Bostock	20.25	79.75	Gorup-Besanez, Physiolog. Chemie, 1865, p. 581.
Prösch	38.60	61.40	Do.
Boyser...........	30.23	69.77	Do.

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[1] The existence of these cases of gelatinous hemorrhagic malacosteon may perhaps explain the statement made by *Rindfleisch* (loc. cit., p. 551), contrary as it is to the experience of all other observers, that the marrow of the bones in malacosteon is actually poor in young medullary cells, and that, apart from the extravasated blood-corpuscles, the gelatinous matrix contains only a few angular bodies resembling small epithelial cells (possibly remains of fat-cells).

Analyses made by	Inorganic matter in 100 parts.	Organic matter in 100 parts.	Remarks.
Lehmann	24.40	75.60	Mean of four analyses—2 femur, 2 ribs.
Von Bibra	60.47	39.53	Mean of three analyses of "senile" (!) malacosteon
Rees	30.21	69.79	Mean of three analyses—Tibia, Rib, Vertebra.
Barruel	29.00	71.00	M. Stiebel, loc. cit.
O. Weber	49.94	50.06	Mean of three analyses.
Huppert	25.71	74.29	
Drivon	29.73	70.27	Mean of two analyses.
Mörs and Muck	36.67	63.33	Do.

The accurate analyses of Mörs and Muck have shown that the loss of lime is greater, proportionately, than that of phosphoric acid, in bones affected by malacosteon. There is not enough of the former to make the so-called basic phosphate ($3CaO,PO_5$), which is usually admitted to be the only form of calcium phosphate normally present in the bones of adults.

Lactic acid has been found in the bones by C. Schmidt, O. Weber, Drivon, Mörs and Muck.

For the condition of the urine in malacosteon, see farther on, p. 224.

As a result of the structural and chemical changes I have just described, the bone-tissue is softened and its density diminished; hence the liability of the bones to be bent or even broken. Fracture is most likely to occur when a bone whose cortex has grown thin without being wholly absorbed is acted on by a fall, a blow, or even a violent movement. Now, as it is only in the very last stage of the disease that the compact cortex disappears entirely—and even then not in all the affected bones at once—we usually find, in advanced cases of malacosteon, fractures and flexions side by side in the same or in different bones. For this reason we cannot accept Kilian's division of malacosteon into two forms, *osteomalacia flexilis s. cerea* and *O. fracturosa.* Those cases in which we find multiple fracture, without flexion, of the bones, belong to other categories of atrophic change, especially to senile wasting of the skeleton, which used formerly to be confounded with malacosteon. The fractures in the latter disease are either partial or complete. Even when complete, the periosteum often remains uninjured and forms a sheath around the wasted fragments. Repair is more or less perfect, according as the disease is in an early or a later stage, the decalcification of the bones not too far advanced, and the patient's general strength not too much reduced. Even at a late period, callus may still be formed, though very slowly, by the periosteum; but the newly-formed tissue does not usually become thoroughly calcified, and a false joint results. Even callus of old standing which has been perfectly consolidated may undergo subsequent softening in the course of the disease.

Even in those bones that are not fractured, the morbid process appears sometimes to recede, and consolidation to take place. We are obliged to infer this from many appearances presented during life, and from the occasional, though very rare, instances of recovery on record. But of the structural phenomena of this process of repair we know nothing.

The changes in the bones give rise to deformities of the skeleton. These deformities usually show themselves first in the trunk, the spinal column, and the pelvis; sometimes, though less commonly, in the thorax.

In the spinal column the lumbar vertebræ are the first to be affected, the dorsal and cervical regions being subsequently implicated. They yield to the weight of the body and are flattened; the entire spine soon becomes appreciably shorter than it was; the body looks shrunken; the head sinks on the breast, the chin resting on the sternum. Kyphoses, kypho-scolioses, and lordoses are produced, the exact form of curvature being determined by the patient's attitude and by the other deformities which react upon the spine. The pelvis undergoes changes of form which are of great importance in relation to pregnancy and parturition; for this reason, as also because the disease itself is most usually observed in pregnant women, they have been very diligently studied. The pelvis is usually compressed from side to side by the heads of the thigh-bones; this, with angular curvature of the pubic rami, causes the symphysis to become beaked and to project forward; the promontory of the sacrum sinks downward and forward into the cavity of the pelvis and approaches the intruding acetabula. When the distortion is extreme, the pelvic inlet is trefoil-shaped.

The deformity of the ribs is not unlike that seen in rickets. They are bent inward, partly by the traction of the lungs, partly by the weight of the patient's body when lying on its side. They are often not merely bent, but broken. The sternum, which is usually much softened, is either arched forward, or concave and drawn in; it is almost always partially fractured at one or more points. The clavicles, too, are not unfrequently broken and distorted.

The distortion of the extremities is also due to fracture and bending of the bones. It obeys no law, and varies with accidental circumstances. The flattening and over-extension of the terminal phalanges of the fingers, to which Charcot[1] has drawn special attention, is in some degree characteristic; it is accounted for by the pressure they sustain when the bedridden patients try to raise themselves on their hands.

The cranial bones are seldom affected. Sometimes, in the very worst forms of malacosteon, they have been found soft and yielding. The bones of the face are still less liable to become involved in the morbid process. Nothing is known of any decalcification or softening of the teeth.[2]

We know very little about changes in other organs occurring in the course of malacosteon. The muscles have been described as flabby, wasted, and in a state of fatty degeneration, occasionally reduced to thin, ribbon-like bands. These changes were always most advanced in the muscles of the lower extremities, in those of the pelvis and back (Stanski, Weber, Chambers), and were ascribed to the degenerative processes which usually result from forced inaction of the limbs. But Friedberg,[3] and still more recently Friedreich,[1] have pointed out that changes of another kind may likewise be detected in the muscles—changes that are active and inflammatory (granular, albuminoid cloudiness, and especially proliferation of the muscle-nuclei); these changes are present, moreover, at a very early period of the disease, before the bones can have been much altered; and thus we are obliged to conclude that the muscles are independently affected in many cases of malacosteon, much as they are in progressive muscular atrophy. These facts indicate the desirability of carefully examining the nervous system in cases of malacosteon—a branch of inquiry which has not as yet been followed. Lastly, I may mention that in a considerable number of cases of this disease, calculi, for the most part composed of phosphate and carbonate of lime and magnesia, have been found in the bladder or kidneys.

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[1] Cf. *Meillet*, Déformations de la Main, etc. Thèse. Paris, 1874.

[2] *Stiebel* (loc. cit.) alludes to it, but I have not been able to find any observations to confirm his statement.

[3] Pathologie und Therapie der Muskellähmung. Weimar. 1858. p. 275.

Etiology and Pathogeny.

Malacosteon is upon the whole a very rare disease. In some localities, as, *e. g.*, in the Rhine Valley, it is more common than it is elsewhere, but by no means common enough to be called endemic.

The disease is pre-eminently one of the female sex, the vast majority of cases occurring in women who have passed through one or more pregnancies. The liability to the disease and its severity are both of them proportionate to the number of times the woman has been pregnant. Moreover, when the disease already exists, its symptoms are always aggravated by each successive pregnancy, so that a connection between malacosteon and the puerperal state cannot be denied to exist. Unmarried women, and women who though married have never conceived, do not appear to be much more liable to the disease than men.

It necessarily follows that malacosteon is usually observed during the period of sexual maturity. To speak more precisely, the frequency of the disease attains its maximum between the twenty-fifth and fortieth year of life. It is an excessively rare thing to see it make its first appearance after the fiftieth or before the twentieth year. The isolated cases that are on record of malacosteon in childhood (Ekmann-Beylard) or during fœtal life (Lobstein) are open to grave suspicion, and may with great likelihood be referred to rickets or some other disease of the bones. So, too, many of the recorded instances of malacosteon beginning in advanced life are probably cases of senile atrophy of the skeleton.

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[1] Ueber progressive Muskelatrophie, über wahre und falsche Muskelhypertrophie. Berlin. 1873. p. 346

As regards the influence of sex, I may mention that Marjolin gives 20 to 1 as the proportion of females to males. Gaspari, 13 to 3 (Bouley, loc. cit.). Beylard found 36 women and 11 men in 47 cases; only 5 of the women had never given birth to a child. Litzmann found 11 men and 120 women in 131 cases; only 35 of the women had never been pregnant. Durham, out of 145 cases, found 13 men and 132 women, 91 of the latter having become affected during pregnancy or just after child-birth. Collineau, among 43 females suffering from malacosteon, found only 14 who had never given birth to a child; of the remaining 29, 14 had had more than 4 children, and 6 had been delivered more than once.

Beylard gives the following statistics in reference to age: In 2 of his cases the disease set in before the age of 20; in 5, between 20 and 30; in 17, between 30 and 40; in 10, between 40 and 50; in 20, between 50 and 60; in 3, after 60. Among Durham's 145 cases the first signs of the disease appeared under the age of 20 in 10 cases, above the age of 50 in 12 cases, while the majority commenced between the 25th and 35th years.

Neither inherited tendency, nor a previous attack of another disease, particularly of rickets, can be proved to exert any influence on the development of malacosteon. The possible influence of heredity rests upon a solitary observation of Ekmann's, who found distortion and fragility of the bones in three successive generations of a miner's family in Upland; but the symptoms showed themselves in the children several months after birth, and did not entail any danger to life, so that we may fairly attribute them to rickets. Women who have had rickets in infancy and retain traces of it in their pelvic bones, have repeatedly been known to suffer from malacosteon in after-life. This is not by any means surprising when we consider the great frequency of the former disease, and it furnishes no ground for the belief that the former exerts any influence on the production of the latter, still less for the notion that the two morbid processes are identical. These conclusions have nevertheless been held by many writers on the subject.

Among outward causes, unfavorable hygienic surroundings deserve mention. More especially does residence in a damp dwelling tend to bring on and aggravate the disease. Many cases have been put on record by trustworthy observers in which the first appearance of malacosteon was noticed to coincide with entrance into damp quarters; its arrest, with removal from them. That insufficient food contributes in any way to cause malacosteon is more than doubtful. The demonstrable poorness of the bones in earthy salts naturally suggests the possibility of an inadequate supply of those salts in the food. The prevalence of the disease among pregnant women might be ascribed to the increased consumption of those salts during the pregnant state. Lastly, the occurrence of malacosteon among animals pastured on an arid soil poor in lime might seem to countenance the theory that the disease is brought on by an inadequate supply of lime (Roloff, Stohmann). On the other hand, it has never been proved, nor is it even probable, that the diet of persons attacked by malacosteon is especially poor in lime—that it contains less lime than the diet of other people. Again, though it is quite true, as I acknowledged in speaking of rickets (p. 176), that a simple reduction in the supply of lime in the food may render the bones abnormally brittle, yet this brittleness, so far as more accurate investigations have enabled us to judge, seems to be of an altogether passive kind, analogous to that in senile atrophy. This is undoubtedly the case in many, if not in all instances of so-called malacosteon in the lower animals. Lastly, as regards the increased consumption of nutrient matter during pregnancy, it is not easy to see why the increased demand for lime should not be met by an increased supply, in exactly the same way as the increased demand for other mineral matters is satisfied.

The anatomical evolution of malacosteon teaches us that the disease is made up of a medley of active and passive processes. It begins with active congestion and proliferation of corpuscular elements; the initial changes in the bones presenting a certain resemblance to those in inflammation. These facts are quite in harmony with the commencement of the disease during pregnancy and in the bones of the pelvis; for during pregnancy there is a natural (physiological) congestion of the pelvic viscera and even of the pelvic bones; and this may easily become exaggerated till it amounts to disease. The congestion is followed by removal of earthy salts, and finally by complete liquefaction of the osseous tissue. As these changes undoubtedly spread centrifugally from the blood-vessels, as their results are exactly like those produced by an acid, and as an abnormal formation of acid has actually been demonstrated in the affected bones, we are fairly justified in attributing the altered state of the bone-tissue to a perverted condition of the blood—to insufficient alkalinity of that fluid. Of course the blood is never acid during life, though it has been found acid after death; for an acid state of the blood would be incompatible with life. A diminished alkalinity of the blood, on the other hand, might arise in at least two distinct ways. It might result from the hyperæmic state of the marrow of the bones, which (as I pointed out when speaking of rickets) may resemble the splenic tissue, to which it is closely allied, in being prone to generate an excess of certain organic acids when in a state of irritation (*e. g.*, in leukæmia). True, the only acid hitherto detected in malacosteon has been lactic acid; but then no other acid has been looked for. The ultimate cause of malacosteon would thus be the hyperæmia of the medullary tissue, itself induced by pregnancy and other causes. But there is yet another way of explaining diminished alkalinity of the blood. It may be due to insufficient absorption of alkali or to excessive absorption of acid. The former, as I have already pointed out, is not of itself adequate to produce true malacosteon; a supplementary cause would still have to be discovered to account for the hyperæmia and proliferation in the medulla. The latter—increased absorption of acid—would suffice to explain the entire series of phenomena, were it only proved either that acids in general or that some particular acid might excite that active congestion of the medullary tissue which we find in recent cases of malacosteon. Heitzmann, indeed, ascribes this property to lactic acid; he states that he has produced artificial malacosteon by the continued administration of this acid; the disease coming on at once in the herbivora, and after a preliminary attack of rickets in the carnivora. But lactic acid, given for many months together to patients suffering from diabetes, though it may undoubtedly give rise to certain disturbances (cf. section on Pathogeny of Acute Rheumatic Polyarthritis), has never been known to cause softening of the bones. Besides, even the disturbances just alluded to invariably subside when the remedy is discontinued, whereas the course of malacosteon is, with few exceptions, steadily progressive. Again, there is no reason to suppose that the food of patients suffering from malacosteon contains any quantity of lactic acid, and there is a striking absence of such digestive disorders as might be suspected of generating an excess of the acid in the alimentary canal (cf. Rickets). For all these reasons the theory which attributes malacosteon primarily to lactic acid does not appear to rest, so far as our present information will allow us to judge, on any adequate basis. Indeed, it is less plausible than the theory discussed before, according to which lactic acid and perhaps other acids also are generated *by* the morbid process, in consequence of a primary irritation of the medullary tissue, and lead in their turn *to* decalcification of the bones.

Symptoms and Course.

The patient's first complaint is usually of deep-seated, boring or rending pains in those parts of the body which are subsequently found to correspond to the changes in the bones. Those parts are, in most cases, the pelvis and the lower end of the spinal column; more rarely, and usually in those cases only which are independent of pregnancy and childbirth, *i. e.*, those occurring in males or non-pregnant females, the pains may show themselves first in the lower limbs or in the chest also. They are sometimes localized, sometimes general; at first they are usually intermittent and are aggravated by movement, relieved by rest. Pressure on the bones in the painful region or on particular points of the bones causes pain, so long, at all events, as the malady is actively progressive. Hence the women, in whom the pelvic bones are the first to be attacked, often complain that pain is brought on by sitting or lying down in a particular position, and find themselves obliged to change their attitude frequently.

The pains are speedily associated with a sense of weakness and fatigue. Movement gradually becomes more and more laborious, and the patient can only walk with great exertion, or, at a later period, only with the help of crutches or the arm of an attendant. At the very beginning of the malady in pregnant women or those who have just been delivered, a characteristic symptom is the patient's staggering, uncertain gait; her legs are far apart from each other, and she seems unable to abduct her thighs.

Another, but much less common symptom in patients of the female sex is the increase of nervous excitability ("susceptibilité nerveuse") to which both Trousseau and Lasègue have directed attention. It is recognized by lightly touching or gently stroking the skin over the affected parts, when excessively painful spasm of the muscles ensues. This phenomenon may possibly be connected with the peculiar changes in the muscles described above, and accordingly limited to those cases in which inflammatory changes exist in the muscular tissue.

Malacosteon seldom runs an uninterrupted course. On the contrary, it usually pauses now and then for a variable length of time, every pause being followed by a renewal of the morbid process, due to known or unknown influences, and implicating fresh regions of the skeleton. These exacerbations are all the more likely to occur if the patient's environment continues to be unfavorable, *e. g.*, if she lives in a damp room. Let us take the usual case of a woman attacked by malacosteon in connection with pregnancy. She usually picks up her strength some little time after delivery and returns to her duties, though she finds them more burdensome than they used to be. With every fresh conception the phenomena become more and more severe, the exacerbations being usually attended by fever; but the febrile disturbance never lasts long; on the contrary, the general health, so long as the disease has not reached its most advanced stage, is usually pretty good apart from the difficulty of locomotion. The patient's appetite is good and all her other functions are regularly performed, especially that of menstruation, which is usually normal in the intervals of pregnancy and lactation.

The softening of the bones gradually manifests itself by the occurrence of distortion. Accidental injuries are followed by fracture, partial or complete. The deformities already described make their appearance ; when extreme, they may give rise to the most eccentric alterations in the form of the skeleton. The observation has been made that women become appreciably shorter with each successive pregnancy, their stature being occasionally reduced to one-half of what it was. Every successive delivery is more difficult than previous ones, until at last natural labor is only effected by violent dilatation of the softened pelvis ; or it may be absolutely impracticable, and Cæsarean section has to be resorted to—an operation which has often been performed on women suffering from malacosteon.

From the pelvis and vertebral column the disease usually extends to the thorax, the thoracic deformity giving rise to dyspnœa, palpitation, or asthmatic paroxysms. Obstinate bronchitis may set in, and the patient's general health, hitherto undisturbed, begin to fail ; its failure being commonly accelerated by diarrhœa, which is seldom absent towards the close of the illness. The spinal deformity, moreover, may lead to compression of the cord, with its usual symptoms. Finally, as the extremities become more thoroughly implicated in the morbid process, the patient grows more and more helpless, till she is unable even to change her position in bed. Her limbs are as flexible as wax, yielding to the lightest pressure, and capable of being bent in any direction without causing pain. In the most advanced stage of the disease—to which the stories of "boneless persons," alluded to in the text, refer—the limbs may be so twisted as to bring the feet into contact with the back or head.

It used formerly to be stated that the urine in malacosteon is abundant, markedly acid, and prone to deposit phosphate and carbonate of lime (according to Solly, in four times the normal quantity). These statements are quite untrustworthy, as may be guessed from the fact that phosphatic deposits cannot occur in strongly acid urine. Recent inquirers have very seldom detected any increase in the amount of phosphates (Weber) ; in most cases, no such increase could be demonstrated (Schuetzenberger, Moers and Muck). This want of unanimity may possibly be due to the urine having been examined at different stages of the disease; for it is quite on the cards that in an early stage, while liquefaction of the bones is actually going on, an excessive amount of earthy salts may be eliminated in the urine; whereas, at a later period, this may no longer be the case. Unfortunately, no continuous observations of the urine have as yet been recorded. In one case, very fully reported by Bouley (loc. cit., p. 93) three analyses of the urine were made at considerable intervals; but they are not of much value, as only the percentage composition of the secretion was determined. (On the first occasion the urine had a specific gravity of 1010–1013, contained 3.015 per cent. of solids, and 0.043–0.073 per cent. of phosphates. Nine months later its specific gravity was 1012, and it contained 1.15 per cent. of phosphates.) The quantity of earthy matter got rid of in the urine may also be influenced by the formation of phosphatic deposits and calculi in the urinary organs, an accident which has more than once been observed in malacosteon. Older writers speak also of an excretion of earthy salts in the saliva and the perspiration; and Pagenstecher goes so far as to say that a similar excretion may take place from the bronchial and intestinal mucous membrane, causing catarrh, while the elimination through the kidneys is reduced.

Lactic acid was found in the urine by Moers and Muck in two out of three cases. In one of these, which ended in recovery, the proportion of acid was observed to undergo a gradual decrease as the patient got better, ultimately disappearing altogether from the urine.

The progress of the disease is always extremely slow. Remissions are frequent; indeed, the most common variety of malacosteon, that associated with pregnancy, may remain stationary for years together, provided that conception does not take place. Even that far more rare variety of the disease, which is independent of the puerperal state, runs a very slow and interrupted course; but the intervals of remission are shorter, and the arrest or recession of the disease appears to be less complete. Accordingly, it is of a more continued type, only diversified by exacerbations from time to time. In this latter form, moreover, the disease does not remain confined for so long a time to a few bones (those of the pelvis and the lumbar vertebræ); it extends more rapidly to a greater number.

Duration and Issues. Complications.

Malacosteon usually lasts for years. There is only one case on record in which the disease ran its entire course in three months (C. Schmidt). Its average duration may be set down at from four to six years, and even longer. Many cases have been known to linger on for eight or ten years, and Lobstein has recorded one that lasted for thirteen.

The disease commonly ends in death. The fatal issue may be due to the marasmus attendant on the progress of the malady, or to asphyxia from interference with respiration, or to operations undertaken during delivery, more especially the Cæsarean section. Recovery has unquestionably been known to occur, but it is very rare and exceptional. Roughly speaking, there are barely five instances of true recovery among about one hundred and fifty cases that have been recorded hitherto.

Arthritis deformans may be regarded as by no means a very unusual complication of malacosteon, to judge from the data at our disposal. Inasmuch, however, as the two diseases tend to arise under almost identical circumstances, in women of the poorer class somewhat advanced in years, their coincidence need cause us no surprise. I have already alluded (p. 217) to the affections of the muscular system that occur in connection with malacosteon. Lastly, I ought to mention that, in many cases, a true senile atrophy of the bones has been found to coexist with the changes characteristic of malacosteon; but it is never an easy matter to distinguish between two pathological conditions which ultimately lead to the same or very similar results.

Diagnosis.

So long as pain and impaired power of movement are the only symptoms present, and the bones are neither bent nor broken, we cannot arrive at a certain diagnosis. Still, our suspicions may fairly be aroused, especially in those districts near the Rhine where the disease is not so exceptional as it is elsewhere, if we find a pregnant woman complaining of pain in the back and hips, and of trouble on sitting down or walking about. The discovery of lactic acid, or of an increase in the amount of phosphates, in the urine, might possibly enable us to arrive at a definite diagnosis even at this early stage of the disease. When once, however, some positive deformity, especially the characteristic narrowing of the pelvis, is observed, the existence of malacosteon is no longer doubtful. The only disease capable of producing exactly similar deformities is diffuse cancerous infiltration of the marrow of the bones (*osteomalacia carcinomatosa*[1]), a disease of extreme rarity, which ought to be distinguished from true malacosteon by the greater rapidity of its course and the more profound impairment of the patient's general health.

Malacosteon cannot possibly be confounded with rickets. The former disease is not met with at the same time of life as the latter; moreover, the alterations in the cranial bones—the patent fontanelles and sutures—and the swelling of the epiphyses, symptoms characteristic of rickets, are not met with in malacosteon.

Cases of softening limited to one or several bones of a single limb (Scoutetten,[2] Neill[3]) must not be confounded with true malacosteon; for the latter always shows a decided tendency to spread.

Prognosis.

This is very unfavorable as regards the ultimate issue of the disorder. We cannot, as a rule, look forward to the patient's recovery. The puerperal form, beginning in the pelvic bones, is somewhat more hopeful than the other forms of the disease; for it extends less rapidly, and the intermissions—supposing no fresh pregnancy to occur—are of longer duration.

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[1] *Foerster*, Würzburg. mediz. Zeitschrift, 1861. II. 1. Also *Volkmann*, loc. cit., p. 470.

[2] Gazette Médicale de Paris. 1841. p. 428.

[3] American Journal of Med. Sciences. 1874. Also in Centralblatt für Chirurgie, 1874. No. 31.

Treatment.

The only prophylactic measure that we can recommend to women who already show signs of the disease, is to avoid all risk of renewed pregnancy. For the morbid process itself no remedy is known to exist. Our chief attention must be directed to the improvement of the hygienic surroundings of the patient, especially to her removal from the deleterious influences of damp. Further, we may try to strengthen her general health by appropriate diet and tonics, such as cod-liver oil and iron. Baths may be tried also. We may attempt to compensate for the removal of earthy matter from the bones by giving lime-water or carbonate of lime. To relieve pain, and to prevent, as far as possible, fracture and flexion of the bones, rest, position, mechanical appliances, may be found useful. Any symptoms of a more serious kind must be treated as they arise.

SLIGHT

DISORDERS CAUSED BY CATCHING COLD.

FEBRIS EPHEMERA, HERPETICA, CATARRHALIS
RHEUMATICA, ETC.

SEITZ.

INTRODUCTORY REMARKS.

A few words are required by way of introduction to the following pages. If we consult the case-books of several physicians practising in the same place and among the same class of patients, and who may be credited with the same amount of skill in diagnosis, we shall find a striking difference in the relative frequency of particular affections. One man will register a very large number of cases of some disease, while in the practice of his neighbor the same disease will appear to be rare or altogether absent. This shows that legitimate differences of diagnosis may exist, not so much in very complicated and difficult cases as in those that are quite common and of every-day occurrence. One practitioner will be continually registering cases of ephemeral, catarrhal, rheumatic, and rheumatico-catarrhal fever, while another will hardly allude to them once in twelve months. Nay, if we compare foreign text-books with our own, we shall find some disorders traditionally included in the former which are not so much as referred to in the latter. The most popular of the French manuals (Valleix, Grisolle, etc.) begin with a description of *Febris ephemera* and *F. synocha*, maladies that have no place assigned to them in German hand-books. All this tends to prove that there is a class of comparatively frequent disorders whose specific nature is not yet sufficiently understood to enable all difference of opinion about them to be set at rest. To this category belong a variety of relatively trivial affections undoubtedly provoked by catching cold, and manifesting themselves either in the form of mild febrile paroxysms, or in that of slight local disorders. In the following pages I shall endeavor, as far as possible, to clear up the obscurity which still clings to them.

How we Catch Cold.

That a very numerous class of maladies may be attributed to catching cold, there can be no doubt; even though I am willing to admit that both the public and the profession are only too ready to fall back on this hypothesis, when, as constantly happens, no other is available.

The disorders that really belong to this group are induced by the removal of heat, to an unusual extent, from the external or internal surface of the body. They differ from those due to congelation in that they are not necessarily localized in the part actually chilled, but are usually developed in other—often remote—situations. Hence, the cooling of the surface is not the immediate cause of the disease; it sets up a functional disturbance, and this in its turn excites a morbid process.

The cause in question may be broken up into three factors: a low temperature, air in motion, and moisture. The more thoroughly these factors co-operate in any single instance, the more surely will disease ensue; cooling of the surface being promoted by a constant renewal of the air in contact with it, and by evaporation when the skin is wet with rain or perspiration. Hence, the disorders belonging to this group are most common when the weather is at once cold, wet, and windy; while any one of the above factors, acting alone—*e. g.*, severe cold without rain or wind, a high wind at mid-summer, etc.—does not usually cause any ill effect. It is by no means essential that the noxæ in question should be of great intensity; people occasionally catch cold when the air is both warm and still, as, *e. g.*, when, in hot weather, they uncover some part of the body (neck or chest) which is usually protected. Neither is it needful that the entire surface of the body should be cooled; a few square inches of skin may suffice. For instance, many people catch cold when they have their hair cut in cold weather, *i. e.*, when they expose a small area of skin at the back of the neck to a low temperature, from which it was previously shielded by a bad conductor.

It is generally supposed that a chill is more likely to cause illness when it is sudden, and when the contrast between the temperature of the skin at the moment of exposure (*e.g.*, when it is actually heated), and that of the surrounding atmosphere is great. A cold evening following a sultry afternoon is often blamed for making people ill by the sudden change of temperature. There are, however, many reasons for doubting the correctness of this view. Consider for a moment the violence of the contrast when, in winter, we step out of a room heated to +15° R. (66° F.) into an entrance-hall where the thermometer may be as low as −10° R. (9.5° F.). Consider, too, the experience of patients undergoing the cold-water cure. They never hesitate to expose themselves, while perspiring profusely, to the cold douche or plunge-bath. Many people who are accustomed to sleep without a fire in winter expose themselves, while changing their shirt in the morning, to an extreme contrast of temperature, without getting any harm. All these facts seem to show that in the production of any one of the diseases belonging to the present category, it is not the violence of the contrast, but something else, that is of prime importance. And this "something else" is the length of time during which the noxa is allowed to operate. Momentary exposure to cold, even when the contrast between the temperature of the skin and that of the air is extreme, is seldom followed by illness. Not that I would altogether deny the possibility of diseases being caused by a momentary chill. We know, for instance, that in persons with decayed teeth a puff of cold air on the cheek may bring on a sudden attack of toothache; but, as a general rule, there can be no doubt that exposure to cold is more likely to cause illness in proportion to the time it lasts, and the degree to which the exposed tract of skin is cooled down. The common opinion that a thorough draught in a room is more dangerous than a breeze of equal intensity out of doors, must be regarded as incorrect when expressed in this form. But there is an element of truth in it, nevertheless; for a draught often plays on the body when it is at rest and lightly clad, and may be overlooked for a long time. So, too, the belief that the night air (as in sleeping with a window open) is specially prejudicial may be explained by recollecting that when in bed we are imperfectly covered, one part or other of the body being more easily exposed than by day;

also that the cold air may continue to act for a longer time—for hours together—while we are buried in sleep.

While, on the one hand, it is commonly held that we are especially liable to catch cold when overheated, on the other hand it is equally true that the body offers less resistance to cooling agencies when it is at rest than when the circulation is more or less excited. Every one knows, for example, that sitting long in the open air in cold weather is more likely to bring on a cold than walking about for the same number of hours. The activity of the circulation is kept up by exercise, and does not allow the skin to be cooled down to as low a point as when the body is at rest. Should exercise be pushed till perspiration breaks out, the increased loss of heat owing to evaporation will contribute to cool the surface, and this additional cooling is especially prone to do harm if the activity of the circulation by which the cooling of the skin is retarded be not kept up while evaporation is going on. The traditional belief that exposure to violent extremes of temperature while the body is overheated and perspiring most commonly causes illness, is opposed to the daily experience of water-cure establishments, as I have already pointed out. So much may confidently be affirmed, that sudden cooling of the surface, provided it does not last long enough to chill the skin for good, is not followed by any ill effect.

The milder affections that will be described in the following pages are much more common in childhood and youth than in later years, and we not unfrequently see persons who in early life were extremely liable to such disorders gradually becoming less susceptible as they approach middle life.

As regards the pathology of catching cold, it forms no part of my province to enter minutely into all the theories—most of them reared on very slender foundations indeed—that have been put forth to explain the process.[1] I may, however, be permitted to offer the following hypothesis as that which is most in harmony with our existing knowledge: When the skin is exposed to cold of sufficient intensity and for a sufficient time, the sensory nerves are thrown into a peculiar state, which is propagated to the nerve-centres and reflected by them along certain other channels that are endowed with special susceptibility to this form of stimulus. Should the affected tract be sensory, we get rheumatic pains or neuralgia; should the vaso-motor centre be implicated, alterations in the calibre of the blood-vessels may result (as proved by numerous experiments), especially vascular dilatation (hyperæmia) in particular areas; inflammatory processes may be attributed to a transfer of the stimulus to the trophic nerves,[1] though it must be admitted that our knowledge concerning such nerves is most imperfect; lastly, should the heat-regulating centre be involved and its activity depressed, fever may result. In many persons certain channels appear to be specially open to these reflected stimuli, so that whatever region of the surface be cooled down the same disorder invariably ensues, and the particular organ thus chosen as an habitual victim may fairly be termed a *pars minoris resistentiæ.* It is obvious that a chill may induce a state of morbid irritation in various centres simultaneously and modify the activity of several sets of nerve-fibres at once. We shall find hereafter that a single exposure to cold may be followed not by one only, but by several dissimilar affections arising either simultaneously or in succession. Nay, cases occur in which the central change appears to shift from place to place, one disorder subsiding while still in progress, and a new one springing up elsewhere. The state of excitement induced in the cutaneous nerves by cooling of the surface must be *sui generis*, for irritation of the skin by chemical agents, wounds, and inflammatory processes does not give rise to phenomena of a like kind.

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[1] For such theories the reader may consult: *Wagner's* Manual of General Pathology, pp. 61 and 62. The most recent literature on the subject is referred to in an article by *F. Falk*, in Reichert and Dubois-Reymond's Archiv for 1874, Heft II.

To the old notion that the diseases we are now considering are due to suppression of cutaneous excretion, it has justly been objected that cutaneous excretion is arrested, or at any rate diminished, every time the surface of the body is exposed to cold. But no harm ensues; the emergency is met by the vicarious relations subsisting between the skin and other secreting organs, especially the kidneys. Another argument against the doctrine of suppressed excretion is furnished by the observed fact that people may catch cold when only a very small area of skin—*e. g.*, a few square inches—is exposed. Looking at the matter impartially, it is impossible to believe that an arrest of secretion from so small a surface can possibly give rise to an accumulation of excrementitious products in the blood sufficient to induce disease. Further, we know that an actual arrest of the secretory function of the skin in animals, effected by varnishing them, gives rise to no phenomena in any way resembling those produced in the human subject by catching cold.

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[1] *Heymann*, Berlin, klin. Wochenschrift. Neunter Jahrgang, S. 447.

Period of Incubation.

We are seldom able to ascertain the exact time that has elapsed between the moment of catching cold and the outbreak of the disease. The patient may not have been aware that he was exposing himself to a chill, or the exposure may have been prolonged, or may have occurred repeatedly, *e. g.*, during bad weather, or when the malady results from the abandonment of some article of clothing. In some cases, however, we may be able to determine the period of incubation precisely, *e. g.*, when the patient has been wet through, or has been sitting out of doors in the cold. We learn from such instances that the first signs of illness may show themselves a few hours after the exposure to cold has taken place, sometimes not until one or even two days have elapsed. Accordingly, no maximum and minimum limits can be assigned to the period of incubation. It doubtless depends to a great extent on the nature of the malady developed. Some disorders exclusively dependent on disturbed innervation may show themselves so soon after exposure that they seem almost to coincide with it. Persons predisposed to headache, earache, toothache, etc., may find their slumbering pains aroused at the very moment of exposure to a piercing wind. On the other hand, inflammation of internal organs would seem to require an intermediate process of some sort, so that a relatively longer interval will have to elapse between the exposure to cold and the outbreak of the disease.

The Fever brought on by catching Cold.

We are acquainted with a variety of febrile disorders in which the pyrexia cannot be traced—in harmony with accepted doctrines—to a local process. We know, for instance, that the local changes met with in connection with the infective fevers,—enteric, pyæmia, the acute exanthemata, etc.—cannot be regarded as the *cause* of the fever, since they come long after it in the order of their development. Febrile disturbance not unfrequently results from catching cold; at first, and often throughout its entire course, it is unattended by any local affection. We are nevertheless in the habit of regarding it as a so-called "fever of reaction," *i. e.*, as secondary to some demonstrable or assumed local affection of an inflammatory, catarrhal, or rheumatic character. This arbitrary view is maintained even when the local mischief is strikingly out of proportion to the intensity of the febrile movement; nay, even when the fever sets in long before there is any sign of local disease, or when the local lesion makes its first appearance after the fever has subsided. But, as I have already remarked, cases occur in which the fever runs its entire course without the development of *any* local affection,—when it seems to be a direct result of catching cold; I have experienced this in my own person, and was thus led to attend, for a series of years, to the pathology of the slighter disorders brought on by catching cold. Our knowledge of how we catch cold, and of the true nature of fever, is so imperfect that it would be a mere waste of time to speculate concerning a process which presupposes a deeper insight into both of those subjects. We may infer the existence of some connection between the cutaneous area that is chilled, and the heat-regulating mechanism in the medulla oblongata, in virtue of which the latter undergoes a functional disturbance or enfeeblement of some sort. As to the nature of this connection—whether a disturbance of innervation be directly propagated from the affected region of the skin to the heat-regulating centre, or whether, as others imagine, impeded cutaneous elimination causes a blood-change which, in its turn, influences the heat-regulating apparatus—we know nothing positive. I have already stated the reasons which incline me to prefer the former of these views.

Exposure to cold is very often followed by a slight form of *malaise*, which may be termed a "sub-febrile cold." The temperature seldom rises above 38° C. (100.4° F.); the patient seldom calls in a physician, and refers his symptoms to "mere indisposition" or a "slight cold." The common phrase, "I am unwell, but it is only a cold," usually refers to slight febrile movements of this sort. The chief symptoms are: general *malaise*, such as attends all febrile states; a special disposition to shivering and chilly sensations, to cold hands and feet. Only when the patient retires to bed or sits before a fire does his chilly feeling yield to one of warmth; even then, any exposure to a lower temperature will immediately bring back the former. For instance, if the patient, finding himself uncomfortably warm in bed, throws the bed-clothes off one of his limbs, a creeping sense of chilliness will set out from this part and make its way along the back and the posterior aspect of the limbs over the whole body.

A further peculiarity of this fever and, generally, of the slighter forms of fever brought on by catching cold, is a marked tendency to profuse sweating. No sooner is the patient warm than he begins to perspire with unusual freedom; even if he does not take to his bed and exposes himself to a relatively low temperature, he finds his skin more moist than usual. Owing to this tendency, the urine is usually diminished in quantity, and throws down a reddish sediment of urates.

This febrile state with general *malaise* is often suspected by the patient to be the commencement of some local malady. I remember I used myself to think, when these symptoms came on, that some local disorder adequate to explain the fever must speedily show itself. I recollect that on one occasion, when I was attacked by slight fever after sitting out of doors for a long time in the evening, I went to bed with a firm conviction that I should find myself ill next day, *i. e.*, suffering from some definite local malady. But, to my surprise, the expected catarrhal or rheumatic affection never made its appearance, and I straightway got well. I grant that it is not the rule, but the exception, for such feverish colds to run their entire course without the development of local mischief in some weak spot—some *locus minoris resistentiæ;* but it is often easy enough to prove that the local disease is not at all, or only in part, accountable for the pyrexia. To this point I shall return when I come to speak of the delayed and imperfect localization of a cold.

Local disease of any severity, when brought on by catching cold, is of course attended by its proper fever ("fever of reaction"), and it is sometimes difficult to ascertain how far an existing pyrexia ought to be attributed to catching cold, how far to the presence of localized disease. Sometimes, however, the want of proportion between the intensity of the fever and that of the local mischief, and the absence of any agreement between the two sets of phenomena as regards time of onset, of exacerbation, and of remission, enable us to determine correctly the nature of the febrile movement.

A feverish cold, when uncomplicated, does not usually give rise to any considerable elevation of temperature: what elevation there is, usually takes place towards evening. Sometimes, however, the fever is more intense, without our being able to attribute its intensity to any definite local complication. The symptoms may exactly resemble those of inflammatory fever; the high temperature, quick pulse, flushed face, dry skin, etc., may rouse a strong suspicion in the mind of the observer that some localized inflammation is behind the constitutional symptoms; and yet, on the very next day, or the next day but one, the fever unexpectedly subsides, after having been attended throughout by profuse sweating, just like the milder forms of feverish cold. The graver form that I have just described is interpreted in a variety of ways; it belongs to that group of affections concerning which I remarked in my introductory paragraph that they are registered under different names by different practitioners. German physicians seldom give the name *ephemera* to these transient febrile maladies; they prefer to ascribe them, in a more or less arbitrary way, to a supposed local cause. Should an outburst of *herpes labialis* occur, as it not unfrequently does, some physicians unhesitatingly call the disease a *febris herpetica*, though no one would venture to attribute the acute febrile movement to a trifling eruption that does not show itself till a comparatively late period of the disease. Again, it is not unusual for the physician, when at his wit's end to find a local cause for the fever, to pick out a single symptom—a mere incident of the febrile state,—to place it in the foreground, and to ascribe it arbitrarily to a hypothetical local disorder instead of the fever itself. For instance, a physician brought face to face with a fever unattended by any local mischief, and dominated by the idea that *some* definite local cause must exist, will easily be led into the mistake of referring the symptoms to a gastric catarrh. The patient has lost his appetite; his tongue may be thickly coated; firm pressure on the epigastrium, disagreeable even to a healthy subject, is still more disagreeable to one rendered sensitive by illness. These facts appear to confirm the diagnosis of gastric disease, especially when the observer's mind is already biased in that direction. Another physician is prejudiced in favor of a rheumatic cause; this influences his examination of the patient; he finds support for his view in the abnormal bodily sensations, the languid limbs, the vague and shifting aches of a febrile patient; he does not hesitate to call the attack a *febris rheumatica.* Hence, many physicians may fairly be accused of hobby-riding in the matter of diagnosis; in some case-books the headings "gastric," "rheumatic," "catarrhal," etc., fever occupy much space, while in others they may not even be mentioned.

Uncomplicated feverish colds run a brief, sometimes an ephemeral course. In many cases the fever may become complicated by a variety of local affections, some of which set in early, others late—perhaps long after the fever has reached its height. A renewed exacerbation of the fever may then take place—thenceforward depending wholly on the nature and progress of the local malady.

Feverish Cold with Herpes Labialis.

Febris Herpetica.

Cases occur in which the solitary local affection associated with a feverish cold is an outbreak of herpes on the lips, ears, or buccal mucous membrane. Febrile attacks of this kind have occasionally been described under the name of *Febris herpetica;* Griesinger (in Virchow's Pathologie) defines it thus: "An acute pyrexia which terminates, without further localization, in an outbreak of herpes on the face." There is no reason to think that the trifling eruption is the cause of the fever, especially as the herpes does not always show itself during the progressive stage of the malady, but is often delayed until the fever is subsiding —often, indeed, until it *has* subsided. Another reason against viewing *febris herpetica* as an independent disease is the fact that the eruption is by no means confined, as implied in the above definition, to cases of fever without any other local manifestation; on the contrary, it often accompanies many slight local disorders, such as a cold in the head, a sore throat, cough, rheumatism, etc. It must, however, be admitted that the appearance of herpes during a malady brought on by catching cold is not always a matter of indifference, but that it is often of value in diagnosis. For instance, we find a sharp attack of fever in a child or young person, without any local cause; we suspect the onset of some serious disease, but our anxiety is soon allayed; in a few days there unexpectedly appears on the lips, nose, or cheeks a closely-packed group of vesicles, which at once removes our uncertainty and shows us that we have to do, not with the early stage of one of the more serious fevers, but with a feverish cold which will end favorably in a day or two. The fever described independently in many of our older works, and in the French manuals of the present day, under the name *ephemera,* may be regarded as a member of the present group. Ephemera may be defined as a fever of short duration, brought on by chilling or overheating the body of children and young persons, exhibiting a marked tendency to profuse sweating, and prone to be attended by an outbreak of herpes about the mouth. The term "ephemera" has been generally abandoned by German writers; for a great variety of trifling but distinct affections appear to have been confounded under this name, as may be guessed from the fact that, besides catching cold, many other causes, such as violent emotion, are stated to be capable of producing it.

Local Disorders brought on by Catching Cold, in which Fever is the Dominant Symptom.

The physician is occasionally puzzled by certain febrile disorders, unquestionably brought on by catching cold. A considerable degree of pyrexia is associated with some local affection; but the latter is not sufficiently severe to account for the former. For instance, a high temperature is found to coexist with a cold in the head, and this perhaps not a very bad one. Even if we try to make this account for the fever, arguing from experience that even a slight local inflammation may cause acute disturbance in a susceptible individual, we may be met by the fact that the very same person may, under other circumstances, have had a much worse cold without any attendant fever. Again, we sometimes come across a case of pyrexia in which we can discover nothing but a very slight—doubtfully morbid—increase in the natural redness of the soft palate and tonsils; the febrile excitement being altogether out of proportion to the sore throat. It would be most unsuitable to put these cases into a class by themselves under the name of *Febris catarrhalis.* It would be more correct and less ambiguous, if we believe that a fever is really due to a coexistent catarrh, to term the malady a "febrile catarrh," and to reserve the designation "catarrhal fever" to denote the *character* of the febrile disturbance, without implying that it is a separate disease. These remarks are equally applicable to the terms "*febris rheumatica*" and "febrile rheumatism."

That many of these febrile paroxysms brought on by catching cold are independent of the local affections associated with them is proved by the not unfrequent subsidence of the local disorder *before* the fever. For instance, we meet with a case of fever whose true nature is at first obscure; it may become associated with a cold in the head, or with slight redness of the *velum palati*, or with rheumatic pains. We may fancy our uncertainty relieved by the appearance of these local symptoms. But in a day or two we find to our surprise that the local symptoms have disappeared, and that our uncertainty is as great as ever, unless some fresh local disorder happen to break out—a rheumatic pain, a boil, a labial herpes—and serve to account for the continued presence of the fever. Such abortive outbreaks of local disorders due to cold are not uncommon. They are familiar to the public; we often hear it said that one or other local malady "has not come out properly," and to this the persistence of fever and *malaise* is erroneously ascribed.

Fever brought on by Catching Cold, and attended by a Variety of Local Manifestations, either simultaneous or successive.

There is this peculiarity about many slight cases, that they do not run their entire course in the form of a single, definite, local malady, but manifest themselves as an aggregate of divers affections, either simultaneous or successive, between which it is impossible to establish any natural causal relation. A man catches cold; his illness begins with a rheumatic headache; this soon becomes associated with nasal catarrh or sore throat, possibly with catarrh of the intestines, and finally, perhaps, with an outbreak of herpes labialis. The course of the malady, diversified by these local manifestations, may thus prove not a little puzzling; the original diagnosis has to be unexpectedly supplemented by a second, or even a third, without there being any discoverable connection between them. In this simultaneous or successive development of various morbid processes, which may spring up at intervals of several days, we see evidence in favor of the view that the primary effect of the cutaneous disturbance excited by the chill is an abnormal condition of the nerve-centres, which may set up morbid processes in various regions of the body at various intervals. This view is further supported by the occurrence of a greatly delayed manifestation of certain local affections during fevers brought on by catching cold.

Fever brought on by Catching Cold, with delayed Local Affections.

We meet with cases every day in which a constitutional pyrexia brought on by catching cold is at first unattended by any local process. The public are familiar with the fact. The patient himself is usually of opinion, when his fever has lasted for some days before the appearance of any definite local mischief, that the disease has been passing through a stage of latency; he will ascribe the feverishness and depression that precede a cold in the head to a "latent cold." A theory of this kind is hardly in need of any formal refutation; for a local disease which shows itself, not with, but after the fever, cannot possibly account for the latter; especially when, as sometimes happens, the local disease does not show itself till long after the febrile movement has culminated—perhaps after it has entirely subsided. For instance, the herpes labialis, which is so characteristic of the feverish cold, does not, as repeated experience has convinced me, necessarily appear at any definite stage in the course of the fever. It may break out when the constitutional disturbance is at its height, or when it is subsiding, or even after it is quite extinct. It is a mistake to regard the herpes as a "critical" phenomenon, and to connect it with the remission of the fever.

Treatment of Fever caused by Catching Cold.

A large proportion of the patients who suffer from maladies belonging to this class never have recourse to medical aid at all. They leave their malady to nature, or employ domestic remedies. Their favorite principle is the necessity for diaphoretic measures. "I have caught cold and must get myself to perspire," is a phrase in daily use. There can be no doubt that free perspiration facilitates recovery from such febrile affections, whether uncomplicated or associated with any of the slighter local disorders enumerated above. When the patient, by keeping his bed and taking plenty of hot drink, has got himself into a perspiration, he finds his *malaise*, his chilliness, the aching and languor of his limbs, his rheumatic headache or myalgia, his cough, etc., gradually relieved. A few hours' sweating, however profuse, is not always enough—as is commonly imagined—to cure the disease at once. If the patient quits his bed too soon after having perspired, he may perhaps feel easier than he did; but the *malaise*, the disposition to shiver, etc., are not entirely gone, and may even return worse than ever if he exposes himself to a colder atmosphere. It is usually requisite that the increased secretion from the skin should go on for several days in order that the symptoms in question may permanently disappear. Even if the patient leaves his malady to nature, time will gradually, and for the most part surely, bring relief. It is true that whenever the patient exposes himself to a colder atmosphere, perspiration is checked and his chilliness returns; but the skin again begins to act as soon as he returns to a warm room; in any case, he spends the night in bed, where many hours of warmth promote his recovery. But diaphoretic measures are either useless or positively injurious when they are inappropriately extended to disorders which do not really belong to the present group, *e. g.*, to serious affections of an inflammatory kind, attended with high fever, and not benefited by sweating even when this breaks out accidentally during their course. And yet, forced diaphoresis is very commonly misapplied in this way, especially among the peasantry.

GENERAL
DISORDERS OF NUTRITION.

IMMERMANN.

GENERAL DISORDERS OF NUTRITION.

Introduction.

LITERATURE.—*Thomas Schrenck*, Hæmatologia. sive sanguinis historia. 1743.—*W. Hewson*, Experimental inquiries into the properties of the blood. 1774.—*Thackrah*, An inquiry into the nature and the properties of the blood. 1819.—*Scudamore*, An essay on the blood. 1823.—*Stokes*, Pathological observations, I. 1823.—*Stevens*, Observations on the healthy and diseased properties of the blood. 1832.—*Babington*, Medico-chirurgical transactions, XVI. p. 293 et seq.—*Nasse*, Das Blut, physiologisch und pathologisch untersucht. 1836—*Rees*, On the analysis of the blood and urine in health and disease.—*Lecanu*, Etudes chimiques sur le sang humain. 1837.—*Maitland*, An experimental essay on the physiology of the blood. 1838.—*Magendie*, Leçons sur le sang et les altérations de ce liquide.—*Andral et Gavarret*, Annales de chimie et de physique. T. LV. p. 227. *Andral*, Essai d'hématologie pathologique. 1843.—*Scherer*, Chemische und mikroscopische Untersuchungen. 1843.—*The same*, Haeser's Archiv. Bd. X. S. 121 et seq.—*Becquerel and Rodier*, On the composition of the blood. Gazette Médicale de Paris, V. 1853.—*The same*, New investigations on the blood. 1847.—*Popp*, Untersuchungen über die Zusammensetzung des Blutes in verschiedenen Krankheiten. 1845.—*Wunderlich*, Pathologische Physiologie des Blutes. 1845.—*The same*, Handbuch der Pathologie und Therapie. Bd. I. S. 508 et seq. Bd. IV. S. 518 et seq. 1852 and 1856.—*The same*, Archiv der Heilkunde, I. (1860), p. 97 et seq.—*J. Vogel*, Allgemeine pathologische Anatomie. S. 36 et seq. 1845.—*The same*, in R. Virchow's Handbuch der speciellen Pathologie und Therapie. Bd. I. S. 373 et seq.—*Nasse*, Artikel "Blut" in Wagner's Handwörterbuch, Bd. I. S. 75 et seq.—*Engel*, Anleitung zur Benutzung des Leichenbefundes. 1846.—*Henle*, Handbuch der rationellen Pathologie, Bd. II. S. 57 et seq.—*C. Schmidt*, Charakteristik der epidemischen Cholera. 1850.—*Virchow*, Die Cellularpathologie. 4. Auflage. 1872.—See also the more modern text-books of General Pathology, Special Pathology, Therapeutics, and Physiology.

The Essential Nature and General Characters of Disorders of Nutrition. (Ernaehrungsanomalien.)

The following pages will be devoted to the consideration of a group of morbid states and processes whose position in the domain of general pathology is in many ways a peculiar and exceptional one, and which are accordingly in need of a few introductory remarks. The very term chosen to denote them collectively—"General Disorders or Anomalies of Nutrition"—suffices to indicate this peculiarity, for it is singularly at variance with the usual principles by which our nomenclature of disease is governed. One glance at the latter is enough to show that our nosological classification, and consequently the names given to groups of diseases in our special pathology, are still based in the main on the anatomical seat of the mischief. It is clearly in deference to this principle that most of the diseases with which we are acquainted are designated and arranged as diseases of particular organs, sets of organs, and anatomical apparatuses. Again, while the *generic* position of a disease in our nosology depends, as I have just pointed out, upon its seat, so that we speak of diseases of the lungs, of the stomach, etc., the *specific* characters which mark out its place in the generic group are derived from the typical forms of tissue-change and functional disturbance recognized in general pathology as hyperæmiæ, inflammations, morbid growths, neuroses, etc., and which meet us continually among the disorders of the most various organs.

This classification of disease according to the situation and nature of the morbid process—a speaking witness to the influence of morbid anatomy upon clinical inquiry—is not adopted merely on account of its simplicity and convenience; it is perfectly legitimate from a clinical point of view likewise, so long as a statement of the seat and nature of a disease connotes the essential nature and phenomena of the morbid process. When it fails to do this, however—when the seat and nature of a particular disease do not indicate what clinical observation is obliged to recognize as the most important element in the process—when our clinical conscience does not rest satisfied with assigning the malady, *secundum artem*, to its proper niche in the system—we must look beyond it. Various considerations force themselves upon us, which prompt us occasionally to throw off the rigid fetters of the unitary system of classification and boldly to construct groups of morbid processes whose generic characters do not admit of being expressed by the *seat*, nor their *specific* characters by the *nature* of the structural alterations.

Even in the present Cyclopædia, as may be seen by glancing at the Tables of Contents in the different volumes, this liberty has been taken; for, although topographical considerations have been supreme throughout (in the broad grouping of the subjects), they have been set aside without hesitation whenever, as in the case of industrial diseases, infective and toxic processes, etc., the pre-eminent importance of the causal element has been too obvious to be overlooked. By yielding thus much to the claims of clinical expediency, and allowing the etiology of a disease upon occasion to take rank with its localization as a principle of classification, the plan of the present work unquestionably forfeited its logical consistency. Did it gain in usefulness thereby? This question scarcely needs an answer, for almost every contemporary pathological treatise unhesitatingly adopts the same order of exposition, and certainly not at the expense of any deeper insight into the subject.

The group of general disorders of nutrition marks another point in the general plan of this Cyclopædia where, for important clinical reasons, the usual mode of classification is abandoned—where, if we prefer to call it so, a fresh offence is committed against logical consistency. What makes the offence more noteworthy, and what stamps it as exceptional, is the fact that in constructing this group and choosing a generic name for it, not merely the topographical, but the etiological principle of classification likewise, is thrown overboard; for it is not the peculiar seat and nature of the tissue-changes, nor yet any peculiarity of causation, but another—a third element—whose clinical importance has led us to include these various maladies in a common group and to denote them by a generic term.

What is this common element? Why should it assume so prominent a clinical significance? These questions are on the very threshold of our inquiry. Our easiest way of answering them will be to begin with some account of the generic term itself.

The word "nutrition" is employed by physiologists—in so far, at least, as it concerns itself with the vital processes in the more highly organized animals—to denote the exchanges of matter and energy between the blood and the tissues. Accordingly, the words "general disorders of nutrition" will be understood to mean those abnormal states of the organism in which the balance of such exchanges between the blood and the tissues is altered. This, the most general definition of which the disorders of nutrition are susceptible, obviously involves no definite conception of the nature of the disturbing causes; neither does it connote the mode in which, or the place where, the effects of the disturbance manifest themselves by structural changes and clinical symptoms.

While studiedly avoiding any reference either to the causation or to the localization and histological nature of the malady, the term we have chosen lays stress on the existing disorder in the collective exchanges of matter and energy as the leading character of the genus, or, in other words, on the *constitutional* character of the diseases in question; for, no sooner are the normal relations between blood and tissues in any way disturbed, than the constitution of the individual must necessarily begin to suffer, the latter being, after all, only the expression of the vital processes of the individual, in their relation to the mass of matter set in motion, to the velocity and direction of its movement. Inasmuch, therefore, as the expressions, "general disorders of nutrition," on the one hand, and "constitutional disorders, affections, anomalies, etc.," on the other, may be viewed as really synonymous, we shall in future employ them indiscriminately. It is desirable, for a true understanding of the essential nature of the general disorders of nutrition, and of the symptoms they present, that we should pause for a moment to consider more fully the very brief definition given above of "constitution." We shall get a clearer notion of "constitutional disease"—a more specific idea of its characteristics—by connecting it with the physiological acceptation of the term.

We may best attain our object by likening the continuous flow of the vital processes to the current of a river in its bed. Just as in the case of a river we have to distinguish between level, rate of flow, and direction of current, every one of which elements is subject to independent variations—so in different individuals we must recognize that the quantity of matter in circulation, the rapidity and direction of its movement, may all of them vary; so, too (this must be taken for granted), the active energy (*vis viva*, *Wucht*) concerned in the interchange of matter and the form in which that energy may manifest itself. It is not difficult to extend the analogy even farther. Just as one and the same river may at different points of its course present differences of level, a different degree of fall, and a different direction; so, too, the exchanges of matter and energy going on in the same individual may undergo temporary fluctuations. Further, these fluctuations may, like those of water in its bed, be caused partly by internal conditions residing in the moving mass itself, partly by external ones. The constitution of the individual organism may be compared to the sum of all the factors whose joint influence gives the river, in harmony with the properties alluded to above, its characteristic features. The "constitution" represents the form in which the vital processes of the particular organism are fulfilled; it may be mathematically conceived as a sum total capable of variation in time, whose individual factors are represented by the numerical values of the mutually interdependent functions of the organism (measured by the mass, velocity, and direction of the matter moved).

Now, we are taught by Physiology that these numerical values, whether individually or collectively, fluctuate within relatively narrow limits in healthy persons of the same age, sex, etc., placed under similar external conditions. Within these limits lies health; hence, physiology sets up certain average or normal values for the intensity of the individual functions and of the sum total of the exchanges of matter going on—averages from which the ascertained values for particular healthy persons deviate but slightly. On the other hand, physiology teaches us that these normal values may exhibit variations that are considerable but still calculable, *à priori*, whenever the outward conditions of food, temperature, etc., are different, or whenever individuals of different age, sex, etc., are compared with one another.

Lastly, the numerical differences which may be recognized between various healthy individuals, under precisely similar external and internal conditions, authorize us in setting up certain types of physiological constitution; thus we speak of constitutions that are "relaxed," "excitable," "vigorous," "feeble," etc. It cannot indeed be denied that the characters by which these varieties of constitution are distinguished from one another are somewhat flexible and indefinite, so that transitional forms of every degree are not merely conceivable, but actually exist. Again, even our definition of health itself, and of what we agree to call "relatively slight" deviations from the healthy standard, are somewhat arbitrary, so that we actually pass, by imperceptible gradations, from the physiological to the definitely morbid forms of constitution.

The latter, and the constitutional disorders and affections with which they are synonymous, are characterized by *marked* deviations of the vital processes from their normal course—deviations which can neither be attributed to the environment nor to the age, sex, etc., of the individual, but which are in their nature exceptional. What has been said above makes it sufficiently clear that these deviations may concern either the amount of matter in movement, or its velocity, or even its direction; in every one of these elements variations or combinations are possible, which must be collectively and of equal right included in the list of constitutional disorders. So, too, we must insist on regarding not merely permanent, but also transitory deviations of the kind above alluded to, when they overstep a certain amplitude, as constitutional maladies. These may accordingly represent not merely *chronic*, but also *acute* morbid states. From this it necessarily follows that the number of forms assumed by morbid states of constitution is very large, even if we only take the coarsest differences between them into account as a basis of classification. If we nevertheless confine ourselves to the detailed consideration of only a small number of constitutional disorders in the following chapters, this is owing partly to the inadequate state of our existing knowledge in this department of pathological energy, partly to other circumstances that will be more fully discussed hereafter.

Our recognition of the essential nature of the constitutional group of disorders enables us forthwith to determine their general characters. Among these there is one that is pre-eminent, that may be used as a clue in doubtful cases. I allude to the abnormal reaction of constitutionally affected individuals, both to physiological influences and to such noxæ as are adequate to induce disease. This quality—which is, after all, no more than an expression of the fact that in constitutionally affected persons the stability of the dynamic equilibrium of the vital processes is different from that which subsists in health—depends immediately upon the morbid change which the vital processes have undergone in regard to their force and direction, and is therefore intimately bound up with the very essence of every constitutional disorder. For, as a moment's thought will show, we may deduce from the fundamental laws of mechanics the following proposition: "That disturbances of the dynamical equilibrium or permanent state of existing motions, whether as regards changes of velocity or of direction, require for their production disturbing forces of unequal value when, first, the masses moved are themselves unequal; or, second, the existing velocities are different; or finally, third, the directions in which motion is actually taking place differ from one another."

Accordingly, seeing that the reaction of a morbid constitution differs from that of a healthy one (*i. e.*, takes place either more or less vigorously, or in another direction) when it is exposed to the influence of so-called "stimuli," it necessarily follows that cases *may exist* in which the presence of constitutional disorder cannot be recognized at sight; or in which, as we are in the habit of saying, it is, for the time being, *latent*. Supposing no appropriate stimulus to be applied, there may be no sign of disease, since the abnormal course of the vital processes is not necessarily manifested by distinct and constant clinical symptoms. The affected individual may thus present the semblance of perfect health, even for long periods of time. In other cases, again, the existence of disease can only be ascertained by the employment of special, often complicated methods of investigation, or it may accidentally betray itself when some outward influence happens to exalt the morbid tendency to the full stature of disease. All this will cease to appear strange if we reflect on the inadequacy of simple and direct sensory perceptions in other departments of inquiry. A piece of gun-cotton and one of cotton wool are exactly alike; the difference in their chemical constitution is only manifested when they are struck with a hammer or touched with a red-hot iron. To resume a simile which we have dropped, abnormal states of constitution may give as little obvious token of their existence at ordinary times —by altering the patient's own sensations or his outward aspect —as a turbid stream enables us to judge, by mere inspection of its surface, whether it be deep or shallow; this can only be determined by sounding or by jumping into it. So, again, if the sky be overcast, we cannot decide as to the direction in which the clouds are moving—whether it be toward the east or toward the west—without the aid of a compass.

Difficult or even impossible as it often may be for a long time together to recognize the presence of a disorder of the constitution, purely accidental as our recognition of it may ultimately be, still, in by far the majority of cases, a permanent and recognizable "aggregate of symptoms" results from the abnormal flow of the vital processes, or may at any rate betray its presence by frequently recurring paroxysms. Both cases are on the whole easy of comprehension. In the first place we must remember that a man's subjective sense of health and normal aspect always depend in some degree on the integrity of his constitution; any considerable disorder of the latter must sooner or later modify both his feelings and his outward habit. Again, the usually temporary latency of certain constitutional disorders, the frequency of the morbid paroxysms which interrupt the state of seeming health, necessarily result from the abnormal susceptibility of the affected person; influences which leave no trace in the healthy man—nay, even the ordinary vital stimuli—occasionally rising to the position of actual noxæ (causes of disease).

Moreover, the abnormal state of a disordered constitution often shows itself unmistakably in the abnormal symptoms and course of intercurrent maladies of whatever kind, maladies that are not mere local outbreaks of the general disorder, but strictly (because accidentally) complications. This is especially manifest when the accessory malady is in itself a mild one, for more violent forms of every kind of disease come to resemble one another more and more closely in proportion to their violence, and hardly allow any individual differences between them to be discovered. Now, if we bear in mind the definition of a constitutional disorder given above, and look at the accessory complication as a force of variable (usually considerable) intensity which disturbs the velocity or the direction of the movement of matter in the system—then the propositions just enumerated will appear to be inevitable consequences, and will at the same time furnish an adequate mechanical explanation.

As regards the properties common to all the local manifestations of constitutional disease, they will best be described and illustrated at a somewhat later stage.

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General Pathogeny.

While a right understanding of the essential nature of the general disorders of nutrition and of their clinical features is mainly based on a recognition of their *constitutional* character, and is materially simplified thereby, their pathogeny, on the other hand, may be derived more immediately from our ideas concerning nutrition. If a disorder of nutrition, looked at broadly, depends upon a disturbance of the mutual relation between the blood and tissues, it necessarily follows that it may originate either in an abnormal state of the blood, or of the tissues, or of both together. Hence, the pathogeny of the general disorders of nutrition suggests the possibility of their arising in several different ways, and regards any one-sided theory—*e. g.*, that they are all diseases of the blood—as *à priori* unjustifiable. True, the blood is one of the factors in nutrition, and possibly the more important one, but we must beware of thinking that the tissues of the body play a purely passive part in relation to the blood. Notwithstanding the humoralistic views which have once more—and rightly—invaded our pathology [especially as a result of recent discoveries in the domain of inflammation (Cohnheim[1])], no one will venture seriously to contest the activity of the tissue-elements—of the cells—in processes of nutrition, and their capacity for drawing nourishment from the blood (Virchow[2]). Accordingly, we may conclude that although the general disorders of nutrition *may* have their immediate origin in morbid states of the blood—in some disturbance of its quantity or of its composition (*heterometry* or *dyscrasia*)—it does not by any means follow that they *must* always arise in this way.

Indeed, clinical experience and anatomical inquiry agree in furnishing support to this view. In a certain proportion of undoubtedly constitutional maladies or general disorders of nutrition, a heterometry (alteration in quantity) or dyscrasia (change of composition) of the blood may be proved to exist, and to be the cause of the disturbance in the patient's general health, and of the existing local morbid symptoms. In other cases, again, whose truly constitutional character is quite as certain, we nevertheless fail to obtain proof of heterometry or dyscrasia of the blood; and unless we assume the possibility of changes of so refined a character in that fluid as hitherto to have eluded observation, we are clearly bound to attribute such cases to an abnormal state of the tissue-elements or cells (as consumers of the blood).

But this view does not rest solely on the negative results of our examination of the blood; there are positive grounds for it as well. Foremost among these is the fact that in the cases of constitutional disease of which we are now speaking, no constant relation can be made out between the normal supply of blood to individual tissues, and the frequency with which structural and functional changes occur in them. So, too, the local changes are not always associated with, or ushered in by, demonstrable disturbances of circulation (hyperæmia or anæmia, acceleration or retardation of the blood-stream); on the contrary, they are often utterly independent of the circulation, which offers no peculiarity capable of explaining the localization of the morbid process. On the other hand, there are many cases in which the manifestations of a constitutional disorder are obviously localized in organs or tissues—not, indeed, distinguished by any peculiarity of vascularization, but by their exposed position, which renders them liable to injury. These facts, taken together, make it very likely that the constitutional character of many diseases is determined by an abnormal state of the tissue-elements; that there exist general disorders of nutrition whose *primary* seat is not in the blood, but in all, or, at any rate, in a great part of the remaining tissues.

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[1] *Virchow's* Archiv. XL. 1.

[2] Cellularpathologie. 4 Aufl. 1871. p. 142.

But even when we succeed in demonstrating changes in the quantity or composition of the blood, this is not enough to prove that the blood really is the starting-point of the constitutional disorder. For since the blood, besides supplying the tissues with pabulum, also receives from them the products of cellular metamorphosis, it is always possible that, owing to a morbid state of all or the majority of the tissues, a secondary heterometry or dyscrasia of the blood may be induced. The latter would then be, not the cause, but the consequence, of an existing constitutional disorder; and there is good reason to believe that it really is so in some instances (*e. g.*, in diabetes mellitus). This would furnish us with an instance of the secondary localization of general disorders of nutrition in the blood—contrasted, in respect to its pathogeny, both with the more usual form of secondary localization in the tissues, and with that of primary localization in the blood.

Wholly distinct from the condition just described, in which a morbid state of the blood originates in a previous constitutional disorder, is the very common event (to be considered more fully on p. 268) of a local idiopathic disease of some organ, secondarily affecting the blood, and through it the constitution. My reason for mentioning it here is merely to guard against any misinterpretation of my previous statements; for it is clear that any disorder of nutrition arising in the last-mentioned way must belong to the group of blood-diseases, since it is *through* the blood that the primary local malady induces disturbance in the system as a whole, the blood itself being the first seat of the *generalized* disorder.

General Etiology.

Although, as I have already pointed out, the group of "general disorders of nutrition" owes neither its name nor its clinical *raison d'être* to etiological considerations, still a brief inquiry into the causes of constitutional disease is not only desirable, but in a measure indispensable to the general plan of the present cyclopædia. It will serve to explain why only a few constitutional disorders are dealt with in the following chapters, the great majority being described in other parts of the work. The following observations will make this remark more clear.

General disorders of nutrition, like other maladies, are due partly to external, partly to internal, causes. The latter are chiefly, though not exclusively, predisposing causes ; the former, exciting causes ; but even this is not specially characteristic of constitutional disease. Finally, the law of reciprocity holds good here as elsewhere. Briefly stated, it is this : that in any individual case, the predisposing and exciting causes stand to each other in an inverse arithmetical ratio.

Looking more narrowly into the *external* causes of constitutional disease, we find certain differences peculiar to its individual forms—differences which may be made the basis of a classification.

For many constitutional maladies we can prove that the morbid change in the nutritive processes is directly due to infection or intoxication—to the introduction of a specific poison into the system, or, to speak more accurately, into the blood. The constitutional diseases of an infective and toxic character which are thus produced (any further subdivision of which would be out of place) are—owing to the pre-eminent clinical importance of the *causal* factor—dealt with independently in another part of the present work, where they are associated with the *local* effects of poisonous agents—the *local* infections and intoxications.

The ensuing chapters, on the other hand, will be mainly devoted to those constitutional disorders, of which it may certainly, or at all events probably, be affirmed that they are *not* of infective or toxic origin. The term "autogenetic anomalies of constitution," proposed by Wunderlich,[1] is not, perhaps, very happily chosen; we cannot imagine their origin to be really spontaneous; but the term may, on account of its brevity, and for want of a better one, be allowed to stand. It should, however, be clearly understood that the influence of *specific* noxæ cannot be certainly excluded in all cases of so-called autogenetic disorder of the constitution; that, on the contrary, there are some such disorders whose position in this respect is doubtful. Finally, it must be added that many infective and toxic processes (*e. g.*, malarial anæmia, the universal fatty degeneration caused by phosphorus) can only be regarded as specific from an etiological, but not from an anatomical or a clinical point of view; for the same anatomical alterations and the same clinical symptoms may arise in other ways as well. It will, therefore, be impossible to exclude all reference to infective and toxic processes from the following chapters; for the two classes of constitutional disease must inevitably overlap each other here and there.

In the main, however, this separation of the "autogenetic anomalies" from the "infective and toxic processes" is fully justified, not merely from the etiological, but also from the strictly clinical (symptomatic and anatomical) point of view. The next question is to ascertain the general character of those external causes under whose influence the members of the former group are usually developed. And here we are at once met by the difficulty of establishing positive criteria for noxæ, whose main feature is a negative one, viz., the absence of specificity. Even apart from this, it is a troublesome business to determine external causes—chiefly because we are often quite in the dark about them—the disorders appearing to arise spontaneously;

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[1] Handb. d. Spec. Path. u. Therapie. Bd. IV. (1856) p. 518.

further, because even those external noxæ which we are able to detect are often merely *exciting*, not *efficient* causes.

These exciting causes are usually the same as those which provoke local idiopathic maladies; among them are wounds, mechanical, thermic, and chemical injuries. Their importance consists, as I have already pointed out, only in their enabling the constitutional disorder, already present in a latent form, to show itself. They are wholly incompetent to produce it. Further, the abnormal element in the operation of these causes, when they act on a constitution already disordered, consists in the seeming disproportion usually observed between cause and effect; a disproportion sufficiently explained by the abnormal reaction of the affected subject (p. 255). Now, it is plain that an acquaintance with such exciting causes of external origin will tell us little, and that little of a wholly indirect kind, concerning the true etiology of a constitutional disease. Nevertheless, the state of our knowledge about a certain number of the general disorders of nutrition is just of this imperfect kind. Lastly, there are some forms which always, or, at any rate, in most cases, originate immediately from internal causes, and with which outward influences have nothing, or hardly anything, to do.

As regards other forms, again, it may be empirically shown that they really are produced by definite external noxæ, which may thus be legitimately viewed as true, *efficient* causes.

And here we observe a marked contrast to the etiology of infective and toxic processes; for in the class of "autogenetic constitutional disorders" the *efficient* causes are not so much the hurtful properties of definite poisons as some deficiency, some inappropriateness, or some excess of the normal vital stimuli (light, air, warmth, food, exercise, etc.). We may imagine the disorder to arise in some such way as this: the vital conditions by which the movement of matter in the organism is mainly determined are in an abnormal state; hence, the machinery by which the latter is regulated sooner or later becomes inadequate to keep the current of the vital processes in its normal bed, or at its normal level, and an abnormal state of the constitution is sooner or later developed; this, like the normal state, has its intrinsic stability, and may outlast the operation of the external cause to which it was originally due. Should the tendency of the external noxa happen to coincide with that of an internal predisposition, we may expect the constitutional disturbance to be all the more obstinate.

In the course of the foregoing remarks, I have repeatedly, though indirectly, been obliged to allude to the latter or internal set of causes. And, in truth, they play a far greater part in the general etiology of the autogenetic class of constitutional disorders than, *e. g.*, in that of the toxic and infective maladies. Nay, we may boldly affirm that in no department of pathology does the influence of internal causes manifest itself so clearly as in this. It is quite true that we are often obliged to rest satisfied with empirical evidence of their power; to make up for this, however, we are sometimes able to look deeper into the connection between cause and effect, and even to formulate that connection in general terms.

The following are the chief internal causes which influence the development of the general disorders of nutrition.

1. *Inheritance.*—Its influence is often unmistakable; sometimes, indeed, so prominent as to throw all other causes—particularly those of an external kind—into the shade. Other forms of constitutional disease, again, show no tendency, or a very slight one, to be transmitted by inheritance. Although we cannot distinguish those constitutional affections which are hereditary from those which are not at all, or but slightly hereditary, by any set of absolute characters, we may still affirm, with some approach to accuracy, that those constitutional disorders which are frequently or usually transmitted are, for the most part, very deeply rooted in the individual constitution, and hence not to be easily eradicated, while the non-hereditary forms more commonly occur as intercurrent morbid processes.

Again, the connection of the latter with external noxæ is usually a far more decided one than that of the former; indeed, external noxæ are usually no more than exciting causes (see my previous remarks on this point). When a constitutional malady is hereditary, it may be inherited from either parent indiscriminately. From this it naturally follows that when both parents suffer from the same anomaly of constitution, the probability of its being transmitted to their offspring becomes almost a certainty. In the more numerous class of cases, where one parent alone is affected, his influence may occasionally be counteracted by that of the other one. This will explain some apparent exceptions to the law of inheritance. But a residue of inexplicable facts is still left, *e. g.*, a whole generation being passed over, the disease reappearing among the grandchildren. It is more common to find only some members of a generation visibly affected, while others are spared. This may sometimes be explained, when the constitutional disorder is limited to one parent, by supposing the qualities of each progenitor to be exclusively transmitted to certain members of their joint offspring; and when this explanation does not seem available, we may take other internal influences into account, *e. g.*, difference of sex between the children. Lastly, the following points are of especial interest: First, the parents need not always exhibit visible signs of their constitutional vice at the moment of conception; a general disorder of nutrition which is latent in the parents, or which has become latent in them, is as capable of being transmitted as one that is apparent. Second, the inherited vice often remains latent in the infant, and does not show itself till a later period—till the age at which it showed itself in the parents. Hence, it follows that age as well as sex may favor or oppose the influence of heredity; that it is more correct to speak of the constitutional vice itself, than of its manifestation, as being subject to inheritance.

Looked at in this light, the transmission of constitutional disease appears merely as a particular case of the general law of inheritance, which amounts, as is well known, to this: that the most essential qualities of the progenitor are represented in the progeny, in so far, at least, as they are not counteracted by other known or unknown influences. Apart from this reservation, which holds good in the domain of physiology as well as in that of pathology, the children represent their parents; not, however, as stiff copies of equally rigid prototypes, but as variable magnitudes whose variations obey the same type. It is not the actual state of the parents at the moment of conception, but their physical life in its entirety, which is reproduced from similar beginnings[1] in their offspring; it is the constitution—with all the natural changes which it undergoes during its development and its decline—that is usually transmitted by the act of procreation. Accordingly, just as a normal constitution is transmitted, so a constitutional vice is repeated in the offspring, allowance being made for the antagonism of other influences; and it is characteristic of inheritance in general that its effects are often delayed in their manifestation—that they show themselves at particular periods of life.

2. *Age.*—The influence of age is often, as I have just pointed out, a mere function of heredity. Sometimes, however, it plays an independent part in causing the development of constitutional disease. Even granting that there exist autogenetic disorders of the constitution that are wholly unconnected with any particular time of life, this only furnishes a fresh illustration of the fact that those disorders possess no common and universal etiological characteristic. We may safely assert that the influence of age is more often manifested in connection with that of inheritance than independently; hence it is that the other features of those constitutional maladies which are associated with particular periods of life correspond to those which have already been alluded to under the head of hereditary transmission. Now, in those cases where age exerts a distinct influence, its influence is not always equally intense; neither does it always reach its maximum at the same time of life. Certain forms of disease are almost exclusively confined to particular epochs; others, again, disobey this rule more often than they obey it. Many are pre-eminently frequent in childhood and youth; others during maturity or advanced life. Finally, the same disorder may present several maxima of frequency, recurring in the same person at stated intervals; or, at any rate, if we represent its frequency graphically, the curve will show several abrupt elevations.

We may take a broader view of the facts if we adhere strictly to our former definition of a constitutional disorder as an abnormality in the course of the vital processes, and bear in mind the physiological diversities exhibited by normal constitutions at different periods of life. The predisposing influence of age may then be anticipated *à priori*—at least, in many cases—by a simple act of comparison. Suppose, for example, that an individual has been affected from an early age by some vice of constitution—*e. g.*, that he has inherited it; suppose, further, that this vice remains latent for a certain interval. We may anticipate, on mechanical grounds, that it will break out when the deviation from the normal course of the vital processes, as regards the mass of matter moved, the rapidity or direction of its movement, happens to fall in with similar changes normally developed in the constitution at a particular time of life, for it is then that the average of health may be overstepped most readily. But age does not always operate, as in the case just mentioned, merely as an exciting cause; on the contrary, it is clear that those constitutional diversities which are proper to particular epochs may themselves be exaggerated by other exciting causes, till they amount to positive disease. The relations empirically ascertained to exist between particular epochs of life and definite disorders of the constitution may thus admit occasionally of a mechanical explanation; but, to render this possible, the intimate nature of the constitutional disorder must itself be a known quantity, comparable with the normal standard of the vital processes. Without this, no mechanical explanation is possible. We are then thrown back on our experience for help in investigating the intimate nature of many affections whose origin is more obscure.

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[1] Cf. *W. His*, Unsere Körperform und das physiologische Problem ihrer Entstehung. Leipzig. 1875. p. 156 et seq.

3. *Sex.*—The relation of sex to the etiology of the general disorders of nutrition is as manifold as that of age. The development of many constitutional disorders is powerfully influenced by sex; others, again, are altogether or mainly independent of it. The influence of sex often coincides with that of inheritance, or with that of age, or with both together. Sometimes it is altogether independent of them. Where its operation can be traced, it may be limited to one sex only. It is an interesting fact, moreover, that sexual predisposition frequently, though not invariably, manifests itself with greater force after puberty.

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The precise nature of its influence is often inexplicable; sometimes, however, it is analogous to that of age—the physiological diversities of constitution in the two sexes, like those of different periods of life, now helping, now hindering existing tendencies to disease, besides involving an unequal susceptibility to other noxæ.

4. *Physiological constitution.*—Those constitutional differences compatible with health, which exist between persons of the same age and sex, are partly the expression of inherited peculiarities, and partly developed in the individual subsequently to conception—during intra-uterine and extra-uterine life—by the various influences of his environment. Accordingly, the influence of physiological constitution on the origin and development of general disorders of nutrition does not simply coincide with that of heredity, but is, to a very considerable extent, independent of it. It may exert a very striking influence on many forms of disease, and the nature of its operation is singularly clear, for certain physiological conditions of the organism, by an imperceptible augmentation of their peculiar features, may easily exceed the somewhat arbitrary limits of health, and, under accidental influences of a very trifling kind, assume an actually morbid character. Hence, we find the various physiological types of constitution running into disturbances of somatic nutrition which only differ from them in degree. Sometimes, again, though we may have empirical evidence of predisposition, the resulting disorder of nutrition is seen to differ from the type of individual constitution, both in quantity and direction, to so great an extent that we find it impossible to trace their causal relationship with any clearness.

5. *Errors of development and pathological processes.*—In an extraordinarily large proportion of cases, general disorders of nutrition arise in persons who are already excluded from the category of perfect health by local errors of development or local morbid processes. That most abnormal states should be liable to—nay, to speak strictly, should inevitably—pass into constitutional disease, is not in any way surprising. For the organs of which the body is built up are not entirely independent as regards their functions and nutrition; they are welded together

into a single organism partly by their anatomical relations, partly by the mediation of the blood and nervous system; and this involves the mutual interdependence of the whole and its several parts. A disturbance of the physiological machinery in any one place or organ, whether it be due to an error of development or to disease, must necessarily affect *all* the nutritive processes and functions of the organism, and modify its constitution. For instance, the "general *malaise*" associated with local maladies—whose gravity and intensity are mainly due to the dignity of the affected part, to the extent, severity, and duration of the affection—forms an integral part of the disease itself, though it is often unduly neglected in the ordinary systematic description of morbid processes (cf. my introductory remarks), at least if we compare the attention it receives with that bestowed upon the cause, situation, and nature of the local lesion. Hence, it is by no means superfluous that I should here insist on this constitutional element in all diseases, not merely for the sake of scientific completeness, but for other reasons of a practical kind also. For, in the first place, the constitutional disorder, which is secondary to the local process—in other words, the objective disturbance of the individual's state—often excites the special notice of the physician even *during* the progress of the local malady, for it often determines the amount of danger to life, and is a principal object of therapeutic interference (Wunderlich[1]). Moreover, the constitutional state often outlasts the local process of which it becomes an independent sequela, claiming as such not merely to be named and classified, but, above all, to be observed and treated. This survival of the constitutional disturbance after its local cause has ceased to operate may, under favorable circumstances, persist throughout the whole of the patient's after-life. It is plain that its disappearance—after its local cause has been removed—must chiefly depend on the degree in which the constitution has been altered, and the self-adjusting power of the organism. Hence, cases may occur in which, owing to the intensity of the former and the inadequacy of the latter, a complete removal of the general disorder of nutrition is impossible.

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[1] Archiv f. Heilkunde. I. 97 (1860).

In this way an alteration, primarily local, may give rise to subsequent constitutional mischief of a lasting kind.

Disorders affecting the organism in its entirety, when already present, may likewise predispose the constitution to ulterior changes, which may then be brought on by relatively trivial exciting causes. Such constitutional disorders occur either as complications of the primary malady, or as sequelæ that outlast it; in either case they have a claim on our attention.

Those anomalies of nutrition which are secondary to local or general diseases often exhibit a special and distinctive character. This is often, so to speak, of a local kind, derived from the association of the primary disease with some particular organ. I allude more especially to a variety of morphological and chemical disorders of the blood, or "dyscrasiæ" which, as *e. g.* the various forms of leukæmia, icterus, uræmia, etc., are etiologically connected with localized diseases (of the spleen, the lymphatic glands, the liver, the kidneys, etc.). For obvious practical reasons, such general disorders of nutrition are best described in connection with the local causes from which they arise; and this rule has not been departed from in the present Cyclopædia. By eliminating this group, as well as that which comprises constitutional disorders of infective or toxic origin, the number of those left is but a fraction of the whole. The residue includes, in the first place, only those autogenetic disorders of nutrition which are idiopathic, *i. e.*, which do not spring as symptoms from a local root; further, those whose symptomatic character has not as yet been universally acknowledged; lastly, a few constitutional disorders of an undoubtedly symptomatic kind. The last-mentioned class includes certain affections which are wholly devoid of local character, and which, owing to their protean etiology, have not found a suitable place in any of the previous volumes of the Cyclopædia. For instance, I have assigned a special chapter to anæmia—a condition of great practical importance—though it is usually symptomatic; this enables its etiology and special symptomatology to be treated as fully as the limits of the present work will allow.

6. *Psychical influences.*—Among the internal causes of general disorders of nutrition we must include influences propagated

from the central nervous system, especially the brain, and arising from some abnormal state of that organ. Depressing emotions more particularly, either alone or in conjunction with other noxæ, exert a decided influence on the development of many constitutional disorders. Little as we have hitherto been able to make out concerning the precise way in which the molecular changes in the brain matter associated with psychical processes may interfere with the general nutrition of the body, still the possibility of this influence has been conclusively established by clinical experience. On anatomical grounds we may conclude that the centrifugal nerve-fibres which set out from the brain, and in a minor degree perhaps the venous blood and lymph returning from the interior of the skull, are, in all likelihood, the means by which psychical disturbances may ultimately be propagated to the constitution and outward habit, and thus give rise to disorders of nutrition.

Anatomical Alterations.

From the definition of the constitutional class of diseases which I have already given, it is abundantly plain that they are not distinguished by any peculiarity, either of situation or of kind, in the histological changes associated with them. On the contrary, the more general features of the latter are only such as show them to be local emanations of a permanent constitutional process. But in this respect there are wide differences between the individual members of the group ; the following points, however, possess a more general, though by no means a universal significance.

1. Alterations in the quantity (*heterometry*) or in the composition (*dyscrasia*) of the blood, the latter being partly morphological, partly chemical. They exist in many, though not in all forms of constitutional disease. These alterations are indicative, now of a primary, now of a secondary localization of the disorder in the blood, and furnish, whenever they are at all marked, conclusive proof of some general disturbance of nutrition.

2. Alterations of the entire habit. These may coexist with

the foregoing, or be independent of them. They are present, as a rule, whenever a general disorder of nutrition is at all severe; when it is less severe, they may be altogether absent. When present, they furnish proof of constitutional disorder no less conclusive than that afforded by marked changes in the blood; nay, they form the anatomical groundwork of constitutional disease even more immediately than do the changes in the blood. I may add that individual forms of constitutional disorder betray their presence by specific alterations of the habit, which thus become pathognomonic and serve to help our diagnosis.

3. Local foci of disease are frequent, though not invariable anatomical symptoms of constitutional processes; sometimes, indeed, they give us the first hint of the existence of the latter (*see* Introduction). The individual focus does not necessarily exhibit a specific character; hence, it rarely suffices, of itself, to prove the existence of constitutional disease. In most cases, the local products, taken separately, are destitute of histological peculiarity; hence, no constitutional disorder can be stated to exist on the testimony of a single focus of local change. On the other hand, we may legitimately infer its existence as the cause of local and demonstrable changes whenever we find multiple foci developed either simultaneously or successively (embolism having been excluded); also, whenever the local tissue-changes are collectively characterized, in a greater or less degree, by homology of position (*homoiotopy*), or homology of kind (*homoiotropy*). Putting this into other words, we may affirm that, 1st, in many general disorders of nutrition, homologous tissues are chosen for the localization of the morbid process; 2d, that in others, the most unlike tissues are involved in the same anatomical change. All the features which we have enumerated as characteristic of the local foci in general disorders of nutrition may easily be deduced from our previous knowledge of the essential nature of those disorders. The multiplicity of foci, more especially, is only a further illustration of an essential tendency of all constitutional disease; viz.: abnormal susceptibility of the tissues to physiological and pathological stimuli, and a resulting predisposition to structural disorders in general. The two other peculiarities, viz.: homology of situation and homology of kind,

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jointly indicate that the equilibrium of the vital processes in constitutions affected by disease, is rendered unstable in certain definite directions. This accounts, not merely for the exalted liability of the tissues to structural change generally, but also for the fact that this liability is more marked in certain directions than in others. Moreover, homology of situation indicates that in certain cases a particular tissue is specially susceptible to all noxæ of whatever order. Homology of kind implies that in certain other cases *all* the tissues of the body, more or less, are abnormally susceptible to some exciting cause that operates in a definite direction.

This brings our detailed examination of the general properties of the local foci of constitutional disease to a close. It serves to complete, from the anatomical side, the rough general outline sketched in our introductory chapter, for it adds a set of more special characters to those more general ones which were there enumerated.

Functional Disturbances.

In addition to the anatomical alterations presented by the general disorders of nutrition, either on post-mortem examination or during life, they exhibit certain functional disturbances that are often clinically characteristic. These disturbances are often manifest when none of the coarser changes in the nutritive processes can be detected either in the general habit or by examination of individual organs. Here again, the reader must bear in mind that it is not by localizing a functional disturbance in a particular organ, nor by determining the nature of the local vice of function, that we can best grasp its constitutional character; but by looking at it from certain other points of view, which are, for the most part, analogous to those enumerated above under the head of anatomical alterations. The following are the chief points that require to be noticed in this place:

1. *Alterations in the subjective sense of health.*—These are often, though not always present. They may generally be said to develop themselves in proportion to the degree in which nutrition is disturbed. They must be ascribed to the reaction

exercised by the altered function of all parts of the organism, through the medium of the centripetal nerves and of the arterial blood, altered both in quantity and composition, upon the percipient centres of the brain. As all the functions are implicated alike, the general feeling of ill-health does not admit of being definitely localized. Its intensity depends partly on the average intensity of the local disorders of function, partly on the excitability of the conducting and percipient nervous organs, partly on the degree in which the blood may be altered; but it is still in need of more thorough analysis.

2. *Alterations in the chemical processes going on in the body* (both as regards their collective magnitude and the principal direction of chemical activity).—In many forms of constitutional disease these alterations manifest themselves by constant symptoms, giving rise partly to anatomical changes of the habit, partly to changes in the objective energies of the organism. They may sometimes be more directly inferred from the altered quantity and quality of the excretions. Sometimes, however, notwithstanding the presence of a well-marked constitutional disorder, we find no material quantitative change in the sum total of the chemical processes, and no appreciable deviation from the healthy standard in the quality of their final products. We must then recollect that our methods of investigation can only furnish data concerning the in-take and out-put, and fail altogether to inform us of the intermediate changes that take place in the system; so that marked deviations from the normal standard may occur in this respect without betraying their existence to us.

3. *Alterations in the function of individual organs.*—These are a necessary consequence of the structural localization of disease. In their mutual relations of coexistence or succession, in their topographical grouping and peculiarity of form, they habitually exhibit features which may be deduced *à priori* from the multiple character of the local foci and their homologies of situation and kind (*vide supra*). Again, it is clear that the local disturbances of function occurring during the course of constitutional disease, as a result of anatomical localization, must react in their turn on the general health when they attain a

certain intensity, and that this reaction may sometimes be so violent as wholly to modify the usual symptoms of the disease for a time.

General Remarks on Diagnosis.

The diagnosis of general disorders of nutrition is difficult or impossible when, for reasons already given, the constitutional malady is for the time being latent, or when its existence is betrayed, in the absence of constant clinical symptoms, only by isolated local outbreaks devoid of any specific character. In cases of this sort, careful inquiry into the patient's history, with especial reference to hereditary tendencies, previous mode of life, and previous symptoms of constitutional mischief, with simultaneous reference to his age, sex, and constitution, will sometimes furnish us with a clue. Our suspicions are likely to be aroused when some intercurrent malady of an ordinary kind, developed without apparent cause in a seemingly healthy person, runs its course with constitutional symptoms of an unusual kind, or terminates in some unusual way; for the contrast between the apparent healthiness of the affected person and the abnormal course of his disorder entitles us, on the principles laid down above, to suspect the existence of some hidden vice of constitution. This suspicion is strengthened when we find local foci of disease, whose anatomical characters are related to one another by homology of situation or of kind (*see* p. 271), developing themselves at short intervals, or simultaneously, at different points, in a person whose previous health appears to have been good. It becomes a certainty when such alterations occur with seeming spontaneity, unprovoked by the usual causes of idiopathic local disease. Finally, the surest proof of constitutional disease, or of a general disorder of nutrition, is furnished by alterations in the general habit (often so characteristic of particular forms of disease), associated with persistent disturbance of the subjective sense of health and of the objective energies. Add the occasional discovery of alterations in the blood, the principal factor in nutrition; add also quantitative or qualitative variations in the composition of the excreta (especially of the urine) greater than those in health, and indicating changes in the force and direction of the molecular movement in the system. From all this it follows that the diagnosis of the general disorders of nutrition, when they are not latent or rudimentary, is not usually beset by any insurmountable difficulties, and that the constitutional character of those affections, notwithstanding individual diversities, may always be ascertained by reference to the principles I have repeatedly enumerated, under which all exceptional instances can easily be disposed of

Course, Issues, and Prognosis.

While the majority of infective and toxic diseases, in conformity with the mode of action of their specific causes, are distinguished by the relative suddenness of their onset and the rapidity of their course, the autogenetic disorders of nutrition begin insidiously, while their farther progress is, as a rule, chronic. To this rule there are, of course, exceptions, just as there are exceptions to the rule among the infective and toxic processes; but the protracted course of most autogenetic constitutional affections, like the contrary behavior of the class I have contrasted with them, is determined by the nature of their external and internal causes; for those outward noxæ, enumerated above as deficiency, unsuitable composition, or one-sided excess of the normal vital stimuli (air, light, food, etc.), usually require time to overcome the physiological resistance offered by the regulating functions of the organism, before they can modify the constitution in the direction of disease. So, too, the disorder, once established, is commonly very slow to yield, and can only be got rid of by very slow degrees. But, as I have already pointed out, those autogenetic constitutional disorders which are chiefly due to external causes are relatively more acute than those induced by causes of an internal kind. Among the latter, those that are hereditary and those that are rooted in anomalies of development are eminently chronic—often coeval with life itself; they may, indeed, remain dormant for a time, but show a marked tendency to recur.

Besides differences in their *duration*, the processes we are about to examine in detail present marked differences in their *course*. Many constitutional diseases are paroxysmal, *i. e.*, they present themselves in a succession of local outbreaks, separated from one another by intervals of absolute latency or apparent health. Others, again, run a continuous course, usually varied by exacerbations due to the localization of the morbid process. In either group the course of the disease as a whole may be progressive, or stationary, or marked by a tendency to spontaneous involution. To which of these three types any constitutional disorder will usually conform, depends, in the first place, upon its causes, whether internal or external. When these causes are in permanent operation the disease is usually progressive; but their removal is not necessarily followed by its spontaneous involution. For should the disturbance in the totality of the vital processes, once set up, have reached a certain degree of intensity, it cannot be allayed by the regulating energy of the organic functions more perfectly than the spontaneous power of self-adjustment will permit; so that if complete recovery be attainable at all, it can only be attained with the help of art. Our art may, under favorable conditions, bring the system back to health, both by annihilating the causes of disease and by aiding the processes of self-adjustment. But, even when it cannot achieve so favorable a result as this, it may still arrest the further progress of the constitutional malady. There still remains, however, a certain proportion of cases, unfortunately too numerous, for which we cannot even suggest, much less apply, any sufficient remedy.

It is abundantly plain that a general disorder of nutrition *may* issue in perfect recovery; and I have pointed out a way in which such an issue can be brought about. I have also shown why, under other conditions, the disorder may terminate in imperfect recovery, or even in death.

In many severe forms of progressive constitutional disease, death is immediately due to an exaltation of the general symptoms, the persistent and progressive disturbance in the function of all the organs, and in the chemical changes going on in the body, attaining an intensity which is incompatible with life. In other cases again, the fatal issue is brought about by individual localizations of the general process. They may cause death at a relatively early period, partly by implicating organs essential to life,—by malignity of position,—partly by malignity of kind. Lastly, the patient may succumb to some intercurrent disease, which, though not genetically connected with the existing constitutional affection, acquires an unusual degree of malignity by coinciding with it. For the irregular course of intercurrent disorders in those who labor under some vice of constitution (cf. p. 257) very often consists in an abnormal malignity, whose causes are sufficiently plain from what I have already stated.

No general rules can be laid down concerning the *prognosis* of general disorders of nutrition. Looked at broadly, it may be favorable or unfavorable; and if unfavorable, it may be so either as regards complete recovery or as regards life. The following general principles may be regarded as established.

All cases in which the external or internal morbific causes admit of being removed offer a favorable prospect, both as regards life and as regards recovery, when they are still in an early stage. The sooner the causes are removed, whether spontaneously or by our art,—the greater the self-adjusting powers of the individual organism—the more assured and speedy will be the cure of the constitutional disorder. The cure may often be hastened by treatment calculated to assist the natural process of repair.

The prognosis, as regards complete recovery, is less hopeful in all advanced cases of constitutional disease, even when their causes admit of being removed. The outlook is still more gloomy when—be the disorder old or recent—its causes can only be combated in their results and not wholly suppressed. This is more often the case with the internal than with the external causes of general disorders of nutrition, especially with heredity, sex, and local anomalies of development; while, on the other hand, the predisposing influence of age may naturally be overcome by time. Finally, there is small chance of complete recovery when, owing to unfavorable circumstances, the needful therapeutic measures do not admit of being adequately carried out, or when the natural power of self-adjustment is weak and hesitating. This is especially true of those cases in which constitutional disease is developed at an advanced period of life, when the sluggish course of the vital processes is often an insuperable obstacle to the spontaneous cure of even trifling disorders of nutrition.

Lastly, as regards danger to life, the prognosis is bad in all very advanced forms of constitutional disease, more especially when we are unable either to remedy the causes of the mischief or to compensate for their operation by our remedies. In such cases the fatal issue is usually not far off, and results simply from the constitutional malady itself. The ultimate prognosis is equally bad in those less advanced cases where the *indicatio causalis et morbi* cannot be fulfilled, and whose course is a progressive one, though the risk of death may be a more remote one. An additional element of extreme gravity is often superadded in the possibility of localization, when the local changes are malignant either in situation or in kind; where this possibility exists, it should be allowed its full weight in relation to prognosis. Lastly, it is always a serious matter when a patient in an abnormal constitutional state is attacked by an intercurrent disease known by previous experience to be malignant when associated with the constitutional state in question, though not of itself dangerous. We must never be misled by the seemingly innocent character of the local malady, still less by the name which correctly indicates its anatomical position, into basing our prognosis exclusively on these data, and thus making it unduly favorable. Such want of prudence is often severely punished by the further course of the disease; nowhere, indeed, is a blind adherence to the routine of morbid anatomy and topographical nosology more likely to bring its votaries into discredit.

General Therapeutics.

The treatment of general disorders of nutrition assuredly demands serious and many-sided attention. It is of great practical interest, owing to their clinical importance. Our first attention must obviously be given to the causes of general disorders of nutrition; secondly, to the individual malady. Moreover, the local manifestations of the constitutional process, and the local disturbances of function they induce, may occasionally require special, systematic treatment. Finally, the usual management of intercurrent disorders must often be seriously modified when the patient's constitution is simultaneously affected.

From the general etiology of autogenetic disorders of nutrition, it follows that the fulfilment of the *indicatio causalis*, and the adoption of prophylactic measures, are chiefly called for when the leading causes are of an *external* kind. Further, the nature of these causes suggests the pre-eminent importance of dietetic rules, whether from a prophylactic or a therapeutic point of view. Diet, in the widest and also the most correct sense of the word, is synonymous with the whole way of life (δίαιτα)—in relation to food, occupation, place of abode, etc. It claims the physician's utmost consideration whenever constitutional disease is imminent or already present; an improvement of the patient's physical environment—perhaps his transfer into a wholly different social and climatic sphere—is unquestionably the most useful, though unfortunately not always practicable, suggestion we can offer. Constitutional diseases, started and maintained by *internal* causes, are much worse off, both as regards prophylaxis and the fulfilment of causal indications by treatment. When we reflect on the nature of those causes which are inherent in the individual, we see that in most cases fulfilment of the causal indication must be out of the question, and the problem of prophylaxis comes to be not so much how to prevent a tendency to disease, as how to check its further development. Only those symptomatic disorders of the constitution which are secondary to curable morbid processes of some other kind form an exception to this rule, since treatment directed against the primary affection will, at the same time, meet the causal indications of the secondary malady, and may under favorable circumstances cure, or at any rate arrest the latter. Finally, as regards prophylaxis, the constitutional affection may best be prevented—while the tendency to it continues in operation—by such measures as would meet the *indicatio morbi* after the disease had already broken out (cf. seq.).

When the *indicatio causalis* cannot be fulfilled, we are thrown back on the *indicatio morbi* as our prime resource. But even when the causes of a constitutional disorder actually admit of being wholly or in part removed, a simultaneous attention to the *indicatio morbi* will make our treatment more certain and speedy. In our choice of means we must, above all, keep the essential object of our treatment, viz., the disordered constitution, well in view. It is clearly our business to restore, as far as may be possible, the strayed current of the vital processes (as regards the mass moved, the velocity and direction of its movement) to its normal channel. The better we understand the essential nature of the constitutional disorder, the more likely are we to discover, by rational methods, *i. e.*, by the aid of physiological and pharmacodynamic principles, an alterative course of treatment which shall antagonize the morbid process. But if the pathogeny of the constitutional disorder be obscure, we are thrown back on our empirical resources; these may be, and occasionally are, successful, but they more often leave us in the lurch.

In cases of this last-named kind the physician is finally reduced to the necessity of limiting himself to the symptomatic treatment of the local manifestations of the constitutional disease, and of the functional disturbances to which they give rise. The fulfilment of the *indicatio symptomatica* is also urgent when the symptoms caused by the localization of the general disease are dangerous or annoying. It should only conform to the general principles by which the treatment of idiopathic local mischief is governed when the *indicatio morbi*, *i. e.*, the treatment of the constitutional state, is beyond the reach both of rational and empirical interference. In all other cases the physician, without underrating the value of appropriate local treatment, must concentrate the resources of his art upon the constitutional disorder itself, for experience has shown that in this way local phenomena of great apparent severity may be made to disappear with amazing rapidity. This is accounted for by the very direct connection between the local mischief and the morbid state of the constitution. The analogy between the way in which many local processes thrive in the congenial soil of a constitutional disorder and certain well-known phenomena of horticulture (*e. g.*, the growth of asparagus, or the artificial cultivation of mushrooms), is too obvious to be missed.

Finally, the continued presence of a general disorder of nutrition modifies the usual treatment of intercurrent maladies in a very striking way. I need hardly point out that the localizing tendency of modern medicine may readily lead the beginner into the habit of treating accurately diagnosticated morbid processes in a routine fashion. On the other hand, we are all of us familiar with the confident assurance of older practitioners, who are enabled by the experience and observation of many years to hit intuitively upon the right remedy at the right moment, more often than the erudite but inexperienced tyro, who leans on his college note-book or his systematic text-book as an abstract and inviolable code. The superiority in this respect of the older school is undoubtedly due in great measure to the circumstance that the detailed examination of the various organs, as it is nowadays practised at the bedside, tends to make us neglect the patient's general habit and his constitution. While the modern physician, armed as it were with an opera-glass, devotes himself to the examination of single parts, the older one, with his unaided eye, while overlooking many a detail, obtains a better view of the subject as a whole. Hence, I feel myself justified in recommending a careful study of the patient's constitution to the present generation of physicians.

If we were to embody the foregoing remarks in a general formula suited to our present purpose, it would take this shape: That the treatment of intercurrent disease in a constitutionally affected subject must be so narrowed or extended as to fit it to the abnormal course of the vital processes, if we would reckon on a favorable issue. This adaptation, like the treatment of constitutional affections itself, may be partly rational—based on a full understanding of the interconnection of the morbid phenomena—partly empirical, for when the true pathogeny of a constitutional disorder is still obscure we must rely on our experience.

The observations contained in the foregoing chapter may perhaps serve to convey a general notion of the disorders I am about to consider in detail, a notion which may be sufficient for theoretical appreciation and practical use, without trenching on the province of subsequent chapters.

Anæmia, Oligæmia, Poorness of Blood.

[*The Ordinary, including the Symptomatic Forms of Anæmia and Marasmus.*]

A general summary of the literature concerning anæmia will be given in the next section—that on Chlorosis—for the two diseases have usually been investigated together. The following works and papers have been specially referred to in the preparation of the account of anæmia.

Introduction:—*J. Vogel*, in *R. Virchow's* Handbuch der speciellen Pathologie und Therapie. Bd. I. (1854). S. 375–447.—*Sée*, Leçons de pathologie expérimentale. 1866. Fascicule I. (Du sang et des anémies).

General Pathogeny:—*Koelliker*, Zeitschrift f. rationelle Medicin. Bd. V. 1846. S. 112 ff.—*R. Virchow*, Verhandlungen der Gesellschaft für Geburtshülfe in Berlin. Bd. I. 1847. S. 379 ff.—*The same*, Gesammelte Abhandlungen. S. 214 ff.—*The same*, Archiv für pathologische Anatomie u. s. w. Bd. II. 1849. S. 595 ff. Bd. V. S. 122—*The same*, Cellularpathologie. IV. Aufl. 1871. S. 191 ff.—*O. Funke*, De sanguine venae lienalis. Diss. inaug. Leipzig, 1851.—*Hirt*, Mueller's Archiv. 1856. S. 174 ff.—*W. Kuehne*, Virchow's Archiv. Bd. XIV. S. 32 ff.—*The same*, Lehrbuch der physiologischen Chemie. 1868. S. 88–90.—*W. Mueller*, Ueber den feineren Bau der Milz. Leipzig, 1865.—*v. Recklinghausen*, Archiv für mikroskopische Anatomie. Bd. II. 1866. S. 137 ff.—*Staedler* und *Holm*, Journal f. praktische Chemie. 1867. S. 42 ff.—*Erb*, Virchow's Archiv. Bd. XXXIV. S. 138 ff.—*Boettcher*, *ibidem*. Bd. XXXVI. S. 342 ff.—*Klebs*, *ibidem*. Bd. XXXVIII. S. 190 ff.—*Eberth*, *ibidem*. Bd XLIII. S. 8 ff.—*Salkowski*, Hoppe-Seyler's medic.-chem. Untersuchungen. Heft III. S. 436 ff.—*Golubew*, Wiener academ. Berichte. Aprilheft 1868.—*Neumann*, Med. Centralblatt. 1868. Nr. vom 10. Octbr.—*The same*, Archiv der Heilkunde. 1869. Bd. X. S. 68 ff.—*Bizzozero*, Gazetta med. Ital. Lombard. 1868, p. 46 ff.—*Hoyer*, Med. Centralblatt. 1869. Nr. 16 u. 17.

Etiology. A. Predisposing Causes:—*Nasse*, Das Blut. 1836.—*Lecanu*, Etudes chroniques sur le sang humain. Paris, 1837.—*The same*, Mémoires de l'académie royale de médecine. T. VIII. 1840. Partie des mémoires. No. 9.—*Denis*, Essai sur l'application de la chimie, etc. 1838.—*Andral et Gavarret*, Recherche sur la quantité d'acide carbonique exhalé par le poumon etc. Paris, 1843.—*Scharling*, Annalen der Chemie und Pharmacie. Bd. XLV. 1843. S. 214 ff.—*Becquerel et Rodier*, Gazette médicale de Paris. 1844. No. 47–51, *Ibidem*, 1846. Nr. 26, 27, 33, 36.—*Zimmermann*, Analyse und Synthese der pseudoplastischen Processe. S. 327. 1844.—*Popp*, Untersuchungen über die Zusammensetzung des Blutes. S. 3. 1845.—*Cazeaux*, Gazette médicale de Paris. C. V. 135 ff.—*Engel*, Zeit-

schrift der Wiener Aerzte. Bd. I. S. 15 ff.—*Scherer*, Verhandlungen der phys.-med. Gesellschaft zu Würzburg. Bd. III. S. 180 ff. 1852.—*Th. L. W. Bischoff*, Der Harnstoff als Maass des Stoffwechsels. Giessen, 1853.—*Wunderlich*, Handbuch der Pathologie und Therapie. Bd. I. S. 536 ff.—*Welcker*, Prager Vierteljahrschrift. 1854. Bd. IV.—*The same*, Archiv des Vereins für gemeinschaftliche Arbeiten. Bd. I. Heft 2.—*H. Beigel*, Untersuchungen über die Harnstoffmengen und Harnmengen u. s. w. Gekrönte Preisschrift. Wien, 1856.—*Panum*, Virchow's Archiv. Bd. XXIX. S. 481 ff.—*Mosler*, Untersuchungen über den innerlichen Gebrauch verschiedener Quantitäten von gewöhnlichem Trinkwasser auf den Stoffwechsel u. s. w. Gekrönte Preisschrift. Göttingen, 1857.—*Geist*, Klinik der Greisenkrankheiten. Erlangen, 1860.—*Vierordt*, Grundriss der Physiologie des Menschen. 1864. S. 503 ff.—*Virchow*, Cellularpathologie. IV. Aufl. 1871. S. 100–143, also 364 ff.

B. Exciting Causes:—I. (*Idiopathic Forms of Anæmia*).—*Chossat*, Recherches expérimentales sur l'inanition. 1843.—*Bidder* und *Schmidt*, Die Verdauungsäfte und der Stoffwechsel. 1852.—*Valentin*, Repertorium. Bd. III.—*Heidenhain*, Disquisitiones criticae et experimentales. 1857.—*Panum*, Virchow's Archiv. Bd. XXIX. S. 241 ff.—*Voit*, Zeitschrift für Biologie. Bd. II. S. 307 ff.—*The same* and *M. v. Pettenkofer*, Sitzungsberichte d. k. bayerischen Academie der Wissenschaften. 10. Nov. 1866.—*Voit*, Zeitschrift für Biologie. Bd. VIII. S. 297, 388.—*Winslow*, Light, its influence on life and health. 1867.—*Fick* und *Wislicenus*, Vierteljahrschrift der Züricher naturforsch. Gesellschaft. Bd. X; Archiv f. wissenschaftl. Heilkunde. Bd. III. S. 136–157. 1867.—*Heaton*, Philosoph. Magaz. 4. Ser. XXXIII. Nr. 224. S. 341–46. 1867.—*Parkes*, Proc. Royal Societ. XV. p. 333 et seq.—*W. Kühne*, Lehrbuch der physiolog. Chemie. 1868. S. 324–26.—*L. Hermann*, Grundriss der Physiologie des Menschen. 1870. S. 233–39.—*Liebermeister*, Du Bois-Reymond und Reichert's Archiv. 1860. S. 520–89. 1861. 28 ff., 1862. 668 ff.—*The same*, Deutsches Archiv f. klin. Medicin. Bd. VII. S. 75., Bd. X. S. 89 ff., S. 420 ff.

II. (*Symptomatic Forms of Anæmia*).—*Vierordt*, Arch. f. physiolog. Heilkunde. Bd. XIII. 1854. S. 271 ff.—*Richard Bright*, Reports on medical cases. 1827. (Cf. also literature of Albuminuria).—*Fr. Oesterlen*, Zeitschrift f. rat. Med. I. Reihe. 1849. Bd. VII. S. 253 ff.—*C. Schmidt*, Charakteristik der epidemischen Cholera. 1850.—*Virchow*, dessen Archiv. Bd. IV. S. 390.—*The same*, Handbuch der spec. Pathologie und Therapie. Bd. I. S. 334 ff.—*The same*, Krankhafte Geschwülste. Bd. I. Cap. XIX. S. 105.—*The same*, Cellularpathologie. 4. Aufl. 1871. Cap. XXI. S. 526 ff.—*Griesinger*, Archiv f. phys. Heilkunde. Bd. VIII. 1854. S. 571 ff.—*O. Wucherer*, D. Archiv f. klin. Medic. Bd. X. S. 379 ff.—*Wunderlich*, Handbuch der Pathologie und Therapie. Bd. III. 3 S. 27–119.—*v. Bamberger*, in R. Virchow's Handbuch d. spec. Pathol. und Therapie. Bd. VI. I. 1. S. 114–126.—*Andral*, Clinique médicale. Bd. III.—*Gendrin*, Leçons sur les maladies du coeur. 1841.—(Cf. the literature of Chlorosis, Leukhæmia, and Pseudoleukhæmia).—*Reil*, Ueber Erkenntniss und Cur der Fieber. I. S. 54. 1799.—*L. Traube*, Charitéannalen. Bd. I. S. 622 ff. Bd. II. S. 19 ff.—*Virchow*,

Handbuch der spec. Path. und Ther. Bd. I. S. 26 ff.—*A. Vogel*, Zeitschrift für ration. Medicin. II. F. Bd. IV. S. 366–88.—*Traube* und *Jochmann*, Deutsche Klinik. 1855. Nr. 46. S. 111 ff.—*Wachsmuth*, De ureae copia in morbis febril. acutis excretae quantitate. Diss. inaug. Berol. 1855.—*S. Moos*, Zeitschrift f. rat. Medic. N. F. Bd. VII. S. 295. 388.—*Redenbacher*, Journal f. Kinderheilkunde. IV. 2, ibid. III. Bd. II. S. 284.—*Brattler*, Ein Beitrag zur Urologie. München, 1858.—*Ranke*, Ueber die Ausscheidung der Harnsäure u. s. w. München, 1858.—*Lemke*, De ureae quantitate in urina febril. experim. quaed. Diss. inaug. Gryph. 1858.—*W. Mueller*, Wissenschaftliche Mittheilungen der phys.-med. Societät zu Erlangen. 1. Heft. 1858. S. 83.—*Uhle*, Wiener med. Wochenschrift. 1859. 7–9.—*Sidney Ringer*, Med. Chir. Transact. XLII. 1859. p. 361.—*J. Vogel*, Archiv f. wissenschaftliche Heilkunde. I. S. 1.—*Behse*, Beiträge zur Lehre vom Fieber. 1864. Diss. inaug. Dorpat.—*Bartels*, Deutsch. Archiv f. klin. Med. Bd. 1. S. 13.—*Liebermeister*, Prager Vierteljahrschrift. Bd. 87. S. 1 ff.—*The same*, D. Archiv f. klin. Medicin. Bd. VIII. 153.—*Leyden*, Ibid. Bd. V. S. 273 ff. Bd. VII. S. 536 ff.—*Senator*, Virchow's Archiv XLV. 1869. S. 351 ff., ibid. L. S. 354 ff.—*The same*, Ueber den fieberhaften Process und seine Behandlung. Berlin, 1873.—*Huppert*, Archiv der Heilkunde. Bd. VII. S. 1 ff.—*The same* und *Riesell*, ibid. Bd. X. S. 329 ff.—*The same*, ibid. Bd. X. S. 503 ff.—*Salkowsky*, Virchow's Archiv. Bd. LIII. 2. 3. S. 209. 1871.

Pathology. Structural Alterations:—*Chossat*, l. c.—*Bidder* und *Schmidt*, l. c.—*R. Virchow*, Gesammelte Abhandlungen. S. 503. 594.—*The same*, Cellularpathologie, 4. Aufl. S. 430.—*The same*, Ueber die Chlorose und die mit derselben zusammenhängenden Anomalien des Gefässapparates u. s. w., Sitzungsbericht der geburtshülflichen Gesellschaft z. B. 1870. S. 17 ff.—*Manassein*, Med. Centralbl. 1868. No. 18.—*Ponfick*, Berl. klin. Wochenschrift. 1873. Nr. 1 ff.—*Perl*, Virchow's Archiv. 1873. Bd. LIX. S. 93 ff.

Special Symptomatology:—I. *Becquerel* und *Rodier*, l. c.—*Vierordt*, l. c.—*Welcker*, l. c.—*A Schmidt*, Archiv f. Anatomie und Physiologie. 1861. S. 545, 587, 675–721; *ibidem*, 1862. S. 428–495, 533–564.—*W. Kühne*, Lehrb. d. phys. Chemie. S. 241–44. 1868.—*Virchow*, Cellularpathologie, 4. Aufl. 1871. S. 197–201.—*The same*, Handbuch der spec. Pathol. und Therapie. 1854. Bd. I. S. 75.—Gesammelte Abhandlungen S. 135 ff.

II. *Hebra*, in R. Virchow's Handbuch der spec. Pathol. und Therapie. Bd. III. 1860. S. 50–51.—*C Schmidt*, Annal. der Chemie und Pharmacie. Bd. LXVI. 1848. S. 342.—*Becquerel* und *Rodier*, l. c. 1852. Nr. 28, 30.—*Virchow*, Handbuch d. spec. Pathol. u. Therapie. Bd. I. S. 182, 195. 1854.—*J. Vogel*, *ibidem*. Bd. I. S. 405-408.—*Chossat*, l. c.—*Liebermeister*, Prag. Vierteljahrschrift, l. c.—*Cohnheim*, Untersuchungen über die embolischen Processe. Berlin, 1872. S. 28 ff.—*J. Bauer*, Zeitschrift für Biologie. Bd. VIII. 1872. S. 567–603.

III. *L. Hermann*, l. c.—*J. Ranke*, Archiv f. Anatomie und Physiologie. 1863. S. 422–450.—*Reinhold*, Hannovers Annalen, Mai, Juni. 1845.—*Bouchut*, De l'état nerveux aigu et chronique. Paris, 1860.—*Cini*, Del sovraeccitamento nervoso nelle sue attinenze colla Chloroanaemia. Venezia, 1861.—*C. Hasse*, in R. Vir-

chow's Pathologie und Therapie. Bd. IV. S. 11-16.—*The same, ibidem*, S. 308-386.—*Marshall Hall*, Medical essays. London, 1825.—*A. Cooper*, Guy's hospital reports. Vol. I. p. 465. 1836.—*Kussmaul* und *Tenner*, Untersuchungen über Ursprung und Wesen der fallsuchtartigen Zuckungen bei der Verblutung Frankfurt, 1857.—*A. Schmidt*, Arbeit aus dem Leipziger phys. Institute. 1867. S. 99 ff.—*Pflueger*, Archiv f. d. ges. Physiologie. Bd. I. 1868. S. 61.—*Nothnagel*, Virchow's Archiv. Bd. XL. 1867. S. 203.—*The same*, Sammlung klinischer Vorträge von Richard Volkmann. Nr. 39—*W. Wundt*, Grundzüge der physiologischen Psychologie. Leipzig, 1874. S. 235 ff., S. 426 ff.—*Romberg*, Lehrbuch der Nervenkrankheiten. 3. Aufl. Berlin, 1857. S. 450 ff.—*Friedreich*, in R. Virchow's Handbuch der spec. Pathol. und Therapie. Bd. V. 2. Abth. S. 71 ff., S. 300 ff.—*Hamernyk*, Physiologische und pathologische Untersuchungen über die Erscheinungen an Arterien und Venen. Prag. 1847.—*Th. Weber*, Archiv f. phys. Heilkunde. Bd. X. 1855. S. 40 ff.—*L. Traube*, Berl. med. Centralzeitung. 1862. Nr. 38, 39.—*Thiry*, Rec. des travaux de la société allemande de Paris. 1865.—*Dohmen*, Untersuchungen aus dem phys. Laboratorium zu Bonn. 1865. S. 83.—*Nasse*, Med. Centralblatt. 1870. Nr. 18.

Treatment:—See the works already referred to: *Bischoff, Mosler, v. Pettenkofer, Voit, Fick* und *Wislicenus, Riesell* und *Huppert, Senator*. Also: *Pokrowsky*, Virchow's Archiv. Bd. XII. S. 476 ff.—*Osw. Naumann*, Archiv d. Heilkunde. Bd. VI. S. 536.—*Liebermeister*, Deutsches Archiv f. klinische Medicin. Bd. III. S. 569 ff.—*Leube, ibidem.* Bd. X. S. 1 ff. und Berlin. klin. Wochenschrift. 1873. Nr. 17.—On the subject of Transfusion: *Prévost* und *Dumas*, Annales de chimie. 1821. T. XVIII. p. 294 ff.—*Dieffenbach*, Die Transfusion des Blutes. Berlin, 1828.—*Bischoff*, Mueller's Archiv, Jg. 1835. S. 347 ff., *ibidem*, Jg. 1838. S. 357 ff.—*J. Mueller*, Lehrbuch der Physiologie. 7. Aufl. 1838. Bd. I. S. 147.—*Brown-Séquard*, Comptes rendus. T. XXXII. p. 855 ff., T. XLI. p. 629 ff., T. XLV. p. 562. Journal de physiologie. I. p. 95 ff. u. p. 666 ff.—*Panum*, Virchow's Archiv. XXVII. S. 240 u. 433.—*P. Scheel*, Die Transfusion des Blutes. 2 Bände. Kopenhagen, 1862.—*Blasius*, Monatsblätter für med. Statistik. Beilage zur deutschen Klinik. 1863. Nr. 11.—*Eulenburg* und *Landois*, Die Transfusion des Blutes u. s. w. Berlin, 1866.—*Landois*, Wiener med. Wochenschrift. XVIII. 1868. Nr. 105.—*Marmonier*, De la tranfusion du sang. Paris, 1869.—*L. v. Belina-Swiontkowsky*, Die Tranfusion des Blutes. Heidelberg, 1869.—*Massmann*, Beiträge zur Casuistik der Transfusion des Blutes. Inaug. Diss. Berlin, 1870.—*Asche*, in Schmidt's Jahrbücher. CL. p. 329 ff.—*Juergensen*, Berl. klin. Wochenschrift. 1871. No. 21.—*Gesellius*, Die Transfusion des Blutes. Leipzig und Petersburg. 1873.—*The same*, Zur Thierbluttransfusion beim Menschen. Petersburg und Leipzig. 1874.—*Leisring*, Schmidt's Jahrbücher. CLVIII. p. 265.—*O. Hasse*, Die Lammbluttransfusion beim Menschen. Petersburg und Leipzig. 1874.—*F. Sander*, Berliner klin. Wochenschrift. 1874. No. 15 and 16.—*Thurn, ibidem.* No. 32.—*Bruegelmann, ibidem.* No. 34.—*Klingelhoefer, ibidem.* No. 36.—*Ponfick, ibidem.* No. 28, and in Virchow's Archiv. Bd. LXII. p. 273.

The somewhat elastic conception of *anæmia* (lack of blood)—or more correctly *oligæmia* (poorness of blood)—when regarded from the point of view of special pathology as a distinct disease, may best be deduced from the nutrient properties of the blood. The blood, as a whole, represents a definite store of potential energy, from which the tissues draw the supplies needed for their growth and their functional activity; and the normal well-being of the entire organism depends primarily upon an adequate supply of blood, *i. e.*, of its functionally effective constituents, to the tissues. Should the circulating blood be deficient in the nutrient matters needed to revivify the tissues, morbid disturbances of function and of nutrition arise sooner or later; and these, together with the primary changes in the blood itself, constitute the aggregate of anatomical and clinical characters known as *anæmia* or lack of blood

Now, of all the constituents of the nutrient fluid, two are of prime physiological importance, viz., *the albuminoid compounds of the plasma* and *the red corpuscles.* These are the chief carriers of the energy on which the vital phenomena of the tissues depend. While the albuminoids of the plasma constitute the pabulum by which the tissues are actually nourished and renewed, the red corpuscles supply them with the oxygen essential to the normal performance of their functions.

Hence, the physiological value of the blood is primarily, though not perhaps exclusively determined by the proportion of albuminoids and red corpuscles contained in it. And any impoverishment of the blood as regards these two constituents must of necessity diminish its physiological value very materially, and expose the welfare of the organism to considerable risk. Accordingly, the term oligæmia is specially employed to denote those morbid states in which, partly by direct examination of the blood, partly by a clinical analysis of symptoms, we are able to infer that the store of plasmatic albuminates and of red corpuscles has been diminished.

The remaining constituents of the blood may, for the present, be left out of account, though it is quite possible that they too may experience a quantitative diminution in cases of so-called oligæmia. This is true both of certain non-azotized ingredients of the plasma, *e. g.*, the fats, and more particularly of the most voluminous constituent of the blood mass, viz., water, which may be so greatly lessened in very many cases of oligæmia as actually to entail an appreciable reduction in the total volume of the blood. Indeed, the very name of the disease suggests this. The terms "anæmia," "oligæmia," "lack of blood," etc., are all volumetric, and in this sense they are still employed in another branch of medicine, viz., general pathology, to denote a diminution in the total volume of the blood. On the other hand, special pathology regards the diminution in the blood mass, dependent on a possible loss of water, as a change which, though usually present and recognizable in cases of anæmia, is rather an accidental complication of the *hypalbuminosis* (diminution of plasmatic albuminates) and the *oligocythæmia* (diminution in the number of red corpuscles), than an *essential* feature of the disease. By laying stress on the two last-named features, as clinically characteristic of oligæmia, we are enabled to include under it those cases in which a reduction in the plasmatic albuminates and the number of the red corpuscles does not happen to be associated with any proportionate decrease in the total volume of the blood. On the other hand, instances of so-called "inspissation of the blood," in which its volume is often greatly reduced by loss of water (*e. g.*, in choleraic diarrhœa), are not usually included under anæmia, because the circulating fluid has not been deprived of any appreciable amount of its albumen and red corpuscles.

While the proportion of water in the blood in the different forms of oligæmia is thus variable, the inorganic salts, standing as they do in a constant relation to the plasmatic albumen, seem always to undergo definite quantitative alterations in oligæmia. According to the well-known researches of C. Schmidt, published a long while ago, there is a constant reciprocal relation between the quantity of plasmatic albumen and that of the inorganic salts. Whenever the blood loses any of its albumen, it takes up an equivalent proportion of mineral salts by diffusion from the interstitial humors, one part of saline matter being absorbed for every nine parts of albumen lost. The salts thus taken up are identical with those normally present in the blood, and they seem to be absorbed in very much the same relative proportions; so that, notwithstanding the slight centesimal augmentation which they collectively undergo, their ratio to one another remains very nearly unchanged. An increase in the percentage of salts contained in the blood must therefore be regarded as another constant feature of pathological oligæmia, and as such it must be associated with the hypalbuminosis of which it is a result—and with the oligocythæmia—among the fundamental characters of the disease.

The remaining constituents of the blood are only negatively concerned in the definition of anæmia, for we only continue to apply this simple term to a morbid state of the nutrient fluid so long as no other coarser alterations are demonstrable in its physico-chemical constitution, or can be indirectly inferred from the symptoms. Thus we shall find it easy to map out, at any rate approximately, the domain of anæmia or oligæmia as a distinct disease; its domain, as we shall see, is a very large one and not very rigidly defined; but it nevertheless admits, to a certain extent, of being designated by a single term.

These introductory remarks on the nature of anæmia will also serve roughly to indicate the point of view from which clinical medicine, in so far as it aims at a practical object, ought to contemplate the disease. The definition given above (which will be retained throughout) includes oligæmia among the general disorders of nutrition, under which head it is accordingly described. It is the special type of that form of constitutional disorder which must inevitably result from a defective state of the nutrient fluid, *i. e.*, from an insufficiency of functionally important elements (viz., albuminates and red corpuscles) in the blood. However widely individual cases of anæmia may differ from one another in their clinical features, there will always be enough points of agreement to enable us to frame a general description of their symptoms and their course.

But it is not so as regards their etiology. In this respect individual cases of anæmia differ widely from one another. This is why, as I have just hinted, the symptoms of anæmia, so uniform in their main features, nevertheless present such remarkable minor differences. It will be my business in the following pages to describe, so far as may be possible, those modalities of the disease which depend on diversities of causation. The limited space at my disposal, however (not to speak of other reasons), will not allow me to go too deeply into details. I may state generally that the differences between the etiological varieties of anæmia, whether in their beginning or in their further course, are not merely *quantitative*—not mere differences in the intensity of the disorder as a whole—but also *qualitative*, the primordial changes in the blood likewise presenting individual variations in degree, which modify the resultant malady in each particular case, independently of the modifications due to the intensity of the disorder as a whole. These quantitative and qualitative differences variously combined furnish so protean a gradation of clinical forms that it would be quite impossible to examine all of them thoroughly and one by one, even though I had much more space at my disposal. Finally, it must be added that our knowledge of the causes of anæmia is often very cloudy and imperfect. Even the way in which many of the causes empirically known to generate oligæmia operate is far from being satisfactorily established or understood. All this, of course, does not contribute to make the subject more transparent.

Before I go on to consider the etiology of anæmia, I think it desirable to say a few words about its pathogeny—to decide generally *how* it may arise—for we cannot address ourselves to the solution of the etiological problem with any prospect of success until we have clearly formulated all the conceivable possibilities and conditions under which oligæmia may arise. That solution will thus be something more than a mere dry enumeration of all the known causes of anæmia. It will include an explanation of the way in which every one of these causes, or groups of causes, operates. Even allowing, as I have just pointed out, that the way in which many noxæ operate is not fully understood by us, and that we only know empirically that they *are* capable of producing anæmia, still we are able to attribute a *modus operandi* to most of them with sufficient certainty to allow of our discussing both cause and mode of operation together. Even when we cannot do this the mere acknowledgment of our imperfect knowledge may stimulate inquiry into the origin of many hitherto obscure forms of the disease.

Pathogeny.

Anæmia is often congenital. It then depends on a primordial disproportion between the available store of functionally effective blood constituents and the tissues they are meant to nourish. More frequently, however, anæmia originates at a later period. Here, too, there is a similar disproportion; but it is not congenital—it is brought on by causes outside of or within the organism.

In acquired anæmia, the store of certain blood constituents, originally adequate, is diminished by disease, and to account for this diminution we are bound to inquire what are the factors on which the magnitude of the store ordinarily depends. These factors are the energy of hæmatopoiesis—of the supply of fresh constituents to the nutrient fluid—on the one hand; on the other, the amount of the losses which the blood simultaneously undergoes from various causes.

Now we know that the volume and centesimal composition of the blood can only be regarded as approximately constant (apart from the transient variations due to absorption of food and drink) in a state of health, in the same individual, and within limited periods of time; for the blood is always undergoing changes whose mutual compensation is exquisitely regulated. The equilibrium of the blood and of its constituents is not statical (to use a term borrowed from mechanics), but dynamical. The material elements of the blood are perpetually being eliminated and replaced by others, the store being kept approximately constant by the adjustment of supply to consumption. Now, in these rapid changes, the functionally important elements of the blood, to whose decrease the phenomena of anæmia are due, viz., the albuminates and red corpuscles, take a very active part; also the water, in so far as its removal is the principal cause of the diminished volume of the total blood mass. At the same time, the physiological value of the blood as the general source of pabulum for the tissues (or, more figuratively, as the "vital juice") is inseparably connected with the perpetual change of its constituent elements, for the nutrition of the tissues is after all a continual robbing of the blood, the tissue-elements abstracting a quantity of albumen and water from the nutrient fluid for the manifold purposes of cell-life. In the same way, individual red corpuscles do not seem able to preside long over tissue-respiration, but are destined to speedy destruction. That an abundant consumption of the water and albuminates of the plasma and of the red corpuscles undoubtedly results from the vital processes is evident from the quantity of water and of derivatives of albumen and hæmoglobin excreted from the body, *e. g.*, urea, uric acid, bile-pigment, urinary pigment,[1] etc.

The rapid consumption of the component elements of the blood implies their restitution in equivalent amount if the permanent stock is not to run short. This is effected partly by ingestion of water, partly by assimilation of food, partly by formation of new red corpuscles, which, there is every reason to believe, originate in the so-called cytogenic organs—the spleen, lymphatic glands, the marrow of the bones, etc. Now, if we consider, on the one hand, the magnitude of the losses which the components of the blood are continually undergoing, and, on the other hand, the extremely complicated mechanism for their renewal, we see at once that disturbances in the dynamical equilibrium of the blood store are very likely to arise, and this from a great variety of causes.

Should the disturbance be considerable in degree—especially if it last for any time—symptoms of oligæmia will be developed. The origin of the disease may thus be traced in all cases to a want of proportion between the consumption and renewal of the functionally important elements of the blood. It follows, too, that the blood store may be diminished in three different ways. The primary phenomenon may be an abnormal acceleration of consumption, or an abnormal retardation of renewal; or, thirdly, accelerated consumption and delayed renewal may exist together. Accordingly, anæmia may arise either by way of *consumption*, when the blood constituents are too rapidly used up; or by way of *inanition*, when their renewal is diminished; or, lastly, in both ways at once. If we compare the state of the blood at any given moment to the volume of water in a lake, the variations which the latter undergoes in consequence of varying outflow and influx will furnish a good image of the different ways in which anæmia may be developed.

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[1] For the artificial preparation of the urinary pigment (urobilin) from hæmoglobin, see *Hoppe-Seyler*, Bericht der deutschen chem. Gesellschaft. VII. 1065.

Some further corollaries from the principles just laid down may legitimately be considered here. In the first place, the singularly unstable dynamical equilibrium of the blood store, to which I have just called attention, enables us to foresee that anæmia must be very common. This anticipation is confirmed by every-day experience, which teaches us that oligæmia, whether symptomatic or idiopathic, is perhaps the most common of all maladies. True, we cannot prove this statement by statistics, simply because anæmia in its milder forms merges imperceptibly into health.

The statement made above, that decided symptoms make their appearance only when the negative variation in the blood store is considerable in degree, does not imply the existence of any definite point at which the impoverishment of the blood amounts to actual disease. Slight variations in the blood store are undoubtedly compatible with health; very considerable ones are followed by unquestionable disease; but, apart from the multitude of cases in which the anæmia is decidedly morbid, we have a still greater number in which the affection is rudimentary, and which blend with the healthy average by a series of imperceptible gradations. By going deeper into this matter, we come to recognize the *predisposing* causes of anæmia, or, in other words, those individual diversities in the blood store which hinder or facilitate the origin, which accelerate or retard the development of the malady, under otherwise similar causal conditions. To this point, therefore, I shall find it necessary to return when I come to speak of the etiology of the disease.

As regards the *exciting* causes of anæmia, it is clear from its pathogeny that they may operate in divers ways. But the etiology of any individual case, whether it be due to a single cause or to a combination of causes, whether its causes be known or unknown, will always be traceable to noxæ acting by way of consumption, or by way of inanition, or by way of both together. Supposing all these noxæ to be empirically known to us—as they often, but not invariably, are—we have to find out in what way they produce anæmia. This problem admits of being definitely solved for many well-known causes of anæmia, while as regards others no solution is at present possible. Thus, we have a very large number of cases of anæmia whose causes and mode of origin are both of them quite clear; we have others whose etiology is only known in part; finally, we have some whose causes are known, while their mode of action is still obscure. These hints are enough to give the reader an idea of the difficulties in the way of tracing out the etiology of many cases of oligæmia. They also show how impossible it is to determine the intimate *nexus* between the phenomena in all cases, for, to do this, perfect insight into the relations between cause and effect is necessary.

We know that we have really fathomed the etiology of a given case, when the *intensity* of the symptoms accords, upon the whole, with that of the predisposing and exciting causes; further, when the *special character* of the disease is in agreement with that of its efficient causes. The former of these criteria is intelligible enough, but the latter requires to be explained a little more in detail.

Oligæmia—in the sense in which the term is employed in special pathology—is a composite disorder of the blood, whose component factors (hypalbuminosis, oligocythæmia, diminution in volume) do not stand in one and the same relation towards its particular causes in every single case. This is obvious when we reflect that the physiological equilibrium of the blood mass—as actually maintained by the healthy organism under the ordinary conditions of its environment—can only be kept up by the operation of a highly complicated mechanism (*vide supra*). The individual parts of this mechanism do not work alike, or at a uniform rate; for neither the consumption nor the renewal of the water, of the plasmatic albumen, and of the red corpuscles, takes place in the same way or with equal rapidity. Now, if the equilibrium of consumption and renewal, as regards one or other of the constituents just enumerated, happens to be relatively unstable for some individual reason — or if some disturbing element is introduced which tends to interfere with one part of the mechanism more than with the others—a blood-change will ensue in which one or other of the partial alterations alluded to above (hypalbuminosis, oligocythæmia, etc.) will at first predominate; even though, as time goes on, the remainder of the mechanism will, as a rule, become secondarily deranged. Inasmuch, moreover, as the various components of the blood are normally both consumed and restored at an unequal rate, we may anticipate that the corresponding partial changes in the blood in anæmia, once developed, will not maintain their mutual proportions as time goes on, nor yet subside at a uniform rate. This anticipation is amply confirmed by experience. Indeed, it may be laid down as a general proposition, in harmony with physiological laws, that of the various components of the blood that are diminished in anæmia, the water is replaced most quickly, the plasmatic albuminates at a slower rate; while the red corpuscles, depending as they do on the activity of the cytogenic organs, are the last to be restored. Hence, it follows that the aggregate symptoms of anæmia, apart from any aboriginal tinge they may have inherited from their causes in any given case, will acquire other special characters as time goes on. The course of the symptoms in every case will depend on the intensity, the duration, and the nature of its causes; and it will continue to be uniform only if the causes retain their original relation to one another.

Having completed these fragmentary observations on the general pathogeny of anæmia, and the circumstances to which the difference between individual cases of the disease is due, I may go on to speak of the etiology of the disease.

Etiology.

Predisposing causes lie at the root of many cases of anæmia, for all persons are by no means equally prone to the disease. Sometimes the malady originates apart from any individual predisposition, as a result of exciting causes capable of making the blood store vary in a negative direction. When a predisposition to anæmia exists, a trifle may provoke an outbreak; on the other hand, noxæ of greater intensity are, of course, capable of producing the disease in persons wholly free from any predisposition to it.

In the following pages the predisposing and exciting causes of anæmia will be considered successively.

A. *Predisposing Causes.*

The predisposing causes of anæmia consist essentially of peculiar states of the constitution, in which the physiological equilibrium of the blood as a whole, though not pathologically disturbed, is nevertheless at a relatively low ebb, or specially unstable. Accordingly, many of these constitutional states pass imperceptibly and without apparent cause into true anæmia, the limit between health and disease being ill-defined. Sometimes the tendency of such "embryonic" forms of the affection to develop into serious disease may be very general, *i. e.*, any sort of cause will suffice to bring on anæmia. In a larger class of cases, on the other hand, actual disease will only arise if the exciting causes be of a special kind and act in a special direction. We shall see hereafter that, under certain conditions, anæmia can only be produced by noxæ that increase consumption; under other conditions, by noxæ causing inanition (cf. p. 292). Again, the special character of the noxæ may bring them into some intimate relation to the constitutional predisposition, *e. g.*, there may be a special tendency to disturbed equilibrium as regards the red corpuscles, or as regards the plasmatic albuminates. We then find noxæ exciting anæmia only if—in virtue of their special nature—they tend to induce oligocythæmia in the former case, hypalbuminosis in the latter.

The diversities of individual predisposition as regards anæmia are chiefly determined by sex, age, and constitution.

1. *Sex.*—We may take it as proved by experience—though not admitting of statistical demonstration—that the tendency to morbid anæmia is much greater in the female than in the male sex. This difference between the sexes shows itself very

markedly in the exceptional frequency with which the rudimentary forms of anæmia, usually known as "weak health," occur among women. They often appear to arise spontaneously. It is likewise true, as a general rule, that the exciting causes of anæmia produce the symptoms of the malady more often and more rapidly (*cœteris paribus*) in women than in men. Of course it must not be forgotten that when the cause is of great intensity, the difference of sexual predisposition disappears (p. 293). I may state, further, that the greater susceptibility of the female sex is especially marked in respect of those noxæ which tend to lessen the proportion of red corpuscles—to generate oligocythæmia—whether by accelerating their destruction or delaying their renewal.

In marked contrast to the development of anæmia in women, rudimentary and apparently spontaneous forms of the disease are far less common in the male sex. Its exciting causes meet with more resistance, and require a longer time to do their work. It is worthy of note, however, that the relative immunity of the male sex seems least marked in relation to such noxæ as tend to produce hypalbuminosis, especially by way of inanition. Lastly (and this is important as regards prognosis), the relatively weaker predisposition of the male sex to oligæmia is associated with a relatively inferior tolerance of the disease. In other words, women are able to bear extreme anæmia longer and better than men.

Is there any theoretical explanation of the different liability of the two sexes to anæmia? Can we account for the sexual diversities that have just been alluded to? We must look to physiology for an answer. We must consider the difference that normally exists between the relative amount and composition of the blood in the two sexes; also the different rate at which the molecular changes incidental to nutrition go on in them. We must recollect that the total volume of the blood bears a smaller average proportion to the body-weight in women than in men (Valentin). A pathological disturbance of the normal ratio between these quantities—a transgression of the average limits that divide health from sickness—would thus seem more likely to occur in the female than in the male. This probably explains the frequency with which rudimentary forms of anæmia are met with in women, as well as the rapidity with which the exciting causes of the disease produce characteristic symptoms in them. Quantitative analysis of the blood in the two sexes has shown that the proportion of red corpuscles is decidedly smaller in women than in men; also that the blood of women is markedly richer in water, and probably — to a trifling extent — in albuminates and salts (Lecanu, Becquerel, Rodier, Nasse, Welcker, Vierordt, et al.). Of these differences the normal oligocythæmia of the female, as contrasted with the polycythæmia of the male, is obviously the most important; it is sufficient of itself to explain the greater liability of the former to such forms of true anæmia as are anatomically characterized by a disproportionate reduction in the number of red corpuscles—by a pathological oligocythæmia. (Cf. what I have said on this subject under Chlorosis.) Estimates of the comparative energy of the molecular changes going on in the system, chiefly based on the quantitative determination of the azotized excreta in the two sexes in health (Lecanu, Bischoff, Beigel, et al.), have shown that the nutritive processes (as measured by the quantity of azotized matter, and the rapidity of its decomposition), are far more active in the male than in the female. The greater consumption of nitrogenous blood constituents — the greater physiological demand for nourishment—in the male, is probably the reason why, notwithstanding the greater relative quantity of its blood, the masculine organism does not seem to have any advantage over that of the female in resisting the influence of inanition, especially when induced by causes which interfere with the renewal of the plasmatic albuminates — why the more intense and extreme forms of anæmia are actually more destructive to the male than to the female.

Welcker's results justify us in assigning 10 : 9 as the normal ratio between the number of red corpuscles in men and in women. Becquerel and Rodier found, as a result of a great number of analyses, that 1,000 parts of blood taken from a healthy man contain, on an average, 141.1 of red corpuscles, while the same quantity of blood from a healthy woman contains only 127.2. The mean amount of albumen in the serum of the male is 69.4; in that of the female, 70.5; the latter has a small advantage in this respect, and also as regards inorganic salts (male, 6.7; female, 7.4), and above all, as regards water (male, 779; female, 791.1). Vierordt gives the following summary (based on the investigations of different inquirers) of the mean proportion of the individual constituents of the blood in the two sexes:

	In the male.	In the female.
Water	784	808
Red blood-corpuscles	152	125
Albumen	54	57
Salts	7	8
Fibrin	3	2
	1,000 parts.	1,000 parts.

I cannot now go more fully into the various methods of investigating the composition of the blood. They are none of them as accurate as might be wished. Notwithstanding their imperfections and the discrepancies between the results obtained by different inquirers, we may regard the greater abundance of colored corpuscles in the male as established. Whether the trifling relative excess of albuminates in the female may not be balanced, so far as the requirements of the organism are concerned, by the greater absolute volume of the blood in the male, must remain doubtful for the present.

The greater activity of molecular change in the male, and the greater consequent need of nutriment, is chiefly inferred from the greater amount (whether absolute or relative) of urea he excretes. Vierordt calculates, as the mean of the results obtained by the various observers enumerated above (the original papers are referred to in the bibliographical catalogue prefixed to the present section), that a man excretes 0.4 grammes of urea in twenty-four hours, per kilogramme of body-weight, while a woman only excretes 0.35 grammes, the ratio between the sexes being 8: 7. The carbonic acid eliminated by the lungs exhibits, according to Scharling, a still greater difference, for the quantity of this gas given off by the male, per unit of body-weight, stands to that given off by the female in the ratio of about 4 : 3. Analogous results were formerly obtained by Andral and Gavarret, who reckon that the male gives off about one-third more carbonic acid than the female.

Before bringing my observations on the influence of sex to a close, I must allude to the special relation that subsists between pregnancy and anæmia. It is generally admitted that pregnant women are peculiarly liable to the disease; there can be no question, moreover, that in one of its forms, hereafter to be described as "progressive pernicious anæmia," it is especially connected with pregnancy (Gusserow[1]). But, even apart from the exceptional instances of progressive pernicious anæmia, we find various degrees of ordinary anæmia, characterized by its usual symptoms, in many pregnant women; so that we are quite justified in speaking of pregnancy as a predisposing cause of the disease. If we go on to inquire what are the exciting causes that provoke true pathological anæmia in pregnant women, we shall find that they are mostly such as interfere with the renewal of the blood —such as operate by way of inanition. Let us now consider the physiological basis of the above assertions.

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[1] Archiv für Gynæcologie. II. (1871). Heft 2, p. 218, seqq.

The blood of pregnant women who are in good health has been shown to contain a relatively large proportion of water; the proportion of red corpuscles, and especially of albumen, is diminished; that of leucocytes moderately increased (Simon, Becquerel and Rodier, Popp, Zimmermann, Kiwisch, Cazeaux, et al.). In other words, the composition of the blood is in all respects brought nearer to the standard of pathological anæmia. But the changes I have just enumerated as normally occurring in the pregnant female are very intimately connected with the increased demand for nutrient matter incidental to pregnancy. If we consider the enormous overgrowth of the uterus which necessarily results from the reception of the fertilized ovum, and the quantity of matter actually surrendered, through the placental circulation, to the embryo, which depends for its supplies on the maternal organism, it is clear that pregnancy must exaggerate the instability of the physiological equilibrium of the mother's blood, and thereby increase her liability to pathological anæmia. More especially may we anticipate the development of this condition when the constituents of the blood are insufficiently renewed; in other words, when the pregnant female is exposed to any of those influences which tend to produce anæmia by way of inanition (*vide supra*). Finally, the whole mass of the blood is physiologically reduced, as regards its percentage composition, to a state of what may be called "temporary impoverishment," a state capable of passing very gradually and imperceptibly, first into rudimentary, then into complete pathological anæmia. We shall come across analogous physiological states in the course of the next few pages, and when we come to consider the exciting causes of anæmia we shall find that certain morbid processes, causally connected with this disease, may be elucidated by reference to the general principles I have just laid down.

2. *Age.*—Although anæmia is very common at all ages, it cannot be denied that the tendency to it is more marked at certain periods of life than at others. Infancy and youth, on the one hand, old age on the other, are specially predisposed to it; while the years of maturity, though far from showing any absolute immunity, are nevertheless comparatively exempt. That the epochs mentioned above are specially predisposed to the disease, is proved not merely by the ease with which it may be brought on, but also by the frequency of its rudimentary forms, and their apparently spontaneous origin. (Cf. analogous facts under the head of "Sex.") How often do we see persons whose constitution was feeble and anæmic during childhood and puberty, growing up into a vigorous maturity; how often, on the other hand, do we see symptoms of anæmia making their first appearance insidiously and without definite cause in persons hitherto robust, during the decline of life. Again, the predisposition due to age displays a characteristic diversity of behavior towards the exciting causes of anæmia, a diversity depending on the way in which those causes operate. By instituting comparative observations at the bedside on a sufficiently extensive scale, we may readily convince ourselves that those noxæ which tend to produce anæmia by way of inanition, *i. e.*, by interfering with the normal activity of sanguification, are peculiarly hurtful in childhood and youth, before the body has reached its full stature; while on the other hand old age, relatively tolerant of privation, is chiefly endangered by sudden increase of consumption. Upon the whole we may conclude (setting aside the more intense causes of anæmia, from which there is no such thing as individual immunity) that middle life, between the twentieth and fortieth years, is most tolerant of those influences which tend to induce anæmia, and best able to withstand them.

Such are the teachings of experience. Like those concerning the influence of sex, however, they may be simply and obviously deduced from a few well-known physiological principles. In the first place, it has been experimentally established that the total volume of the blood in relation to the body-weight is at its greatest during the prime of life; and that it is relatively smaller (in health) in children and old people. Again, the blood in childhood and youth, and also during the decline of life, is somewhat more watery, and contains less solid matter, whether in solution or suspension (Becquerel and Rodier) than the blood of middle age. [The blood of the infant, during the first few days of its existence, must be excluded from this comparison; its composition is in many ways peculiar; for, while its total volume is relatively very small, it is highly concentrated, and especially rich in red corpuscles (Denis, Panum, ll. cc.)]. It follows, accordingly, that the blood of vigorous adults, especially between twenty-five and forty, is superior both in quantity and composition to that of children and old people, and must, therefore, be better able to resist the causes of anæmia. Hence, doubtless, the greater rarity of the rudimentary forms of the disease at this period; hence, too, their frequency before and after it, even without any discoverable cause.

Now, although the differences in the quantity and quality of the blood enable us to understand the varying liability of the organism at different ages to oligæmia, those differences in the nutrient fluid must themselves be regarded as the outcome of certain periodic variations in the molecular movement of matter in the system—variations of a normal kind. Strictly speaking, therefore, we must go back to those variations if we would obtain a deeper insight into the true causes of the different predisposition to anæmia at different ages; especially if we would ascertain how it is that, in youth and in old age, the predisposition varies according to the nature of the exciting causes, as we know from experience that it does. So, too, the greater tolerance for enfeebling influences exhibited during middle life—a tolerance independent of the particular way in which such influences operate—can only be correctly appreciated after a comparative survey of the physiological variations in the rate of molecular metamorphosis throughout life.

It should be noted, in the first place, that these typical variations in the general course of nutrition are not confined to the mass of matter moved, but are likewise manifested in the velocity and direction of its movement. While the mass moved, as may be inferred from the absolute out-put, is at its maximum during the years of maturity, being decidedly smaller in childhood and old age, the rapidity of movement, on the other hand, is far greater in the child than in the adult, and sinks to a minimum as life is drawing to a close.

That the rate of molecular change does really undergo a progressive retardation (apart from a few intermediate fluctuations) may be inferred from the *relative* amount of the excreta (especially urea and carbonic acid) given off by the organism at different periods of life ; for the proportion of the excreta in relation to the body-weight exhibits a steady decrease as years go on. Finally, the direction of molecular movement tends in the adult and in the aged organism merely to maintain the existing state of the tissues, while during childhood and youth it tends to promote their increase ; in the latter period, therefore, we have not merely a perpetual compensation for the losses daily incurred—or nutrition, in the narrower sense of the term—but also what are known as the phenomena of growth. The tissue-elements, or cells, are still under the influence of the "evolutionary impulse" (Wachsthumsreiz of Virchow[1]) conferred on them at the moment of conception ; and both the rapid nutritive changes (*vide supra*), and the luxuriant proliferation of successive generations of cells inheriting the formative *nisus* from their parents, are continually robbing the blood of relatively large quantities of matter for the purposes of nutrition and of growth. The blood of the child and growing youth is thus clearly in a state of "physiological distress ;" so long, however, as supplies are abundantly poured in, this does not pass into pathological anæmia ; but, just as in pregnancy, the somewhat watery condition of the blood and its comparatively smaller volume point to the existence of a certain degree of impoverishment, and it is clear that true anæmia will be at once developed if either the supply of nutrient matter from without be checked, or the vigorous activity of the chylopoëtic and cytogenic apparatus, proper to this time of life, happen in any way to be interfered with. Accordingly, the special liability of childhood and youth to anæmia manifests itself—as has already been stated, though not explained—principally by an extreme susceptibility to all such noxæ as hinder physiological renewal of the blood constituents—or, in other words, operate by way of inanition.

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[1] Cellularpathologie. IV. Aufl. p. 389.

During the prime of life, the stream of nutritive changes is less rapid, and the growth of the organism, though not wholly arrested, is thrust far into the background by the functional and trophic phenomena exhibited by the tissues. The change in the rapidity and direction of movement is associated with a lessened demand for nourishment on the part of the tissues (figuratively speaking, the corpuscular elements are less hungry for blood, *i. e.*, for the nutritive and plastic constituents of the blood), and therefore with an accumulation of these constituents in the blood. Such accumulation is the more apt to occur in health, as the power of adequately restoring those constituents, which are principally consumed in maintaining the tissues in *statu quo*, remains for the time being unimpaired; the digestive apparatus has lost none of its energy, and the cytogenic organs continue to act vigorously. Hence, there results a state of normal plethora, manifesting itself in the quantity and composition of the blood, and also in a greater power of resisting all the causes that tend to induce anæmia.

Lastly, the course of nutrition undergoes a further change during the decline of life, and especially in old age. True, the demands on the blood are less than they were; the body has ceased to grow; the nutrition of the tissues is slow and languid, their corpuscular elements no longer showing much vitality; still, the normal plethora of the blood is no longer to be observed. On the contrary, the condition of the nutrient fluid shows signs of impoverishment, of an impoverishment diametrically opposite to that prevailing in youth, having its root in the insufficiency of the physiological renewal of the blood, and its ultimate causes in the lessened subjective need of nourishment, in the sluggishness of the digestive process, in the functional enfeeblement of the cytogenic organs. The resulting senile involution of the blood causes that fluid to approach more nearly, as regards quantity and composition, to the blood of childhood; from this, however, it differs in the kind of predisposition to oligæmia which it entails; for, whereas the blood of the child is most susceptible to influences operating by way of inanition, that of the old man presents a diminished tolerance of those that operate by way of consumption. For, as the sources from which the blood draws its supplies are beginning to run dry, the symptoms of oligæmia will show themselves the moment the consumption of blood-constituents is unusually increased. The blood-store in old age may be likened to a stagnant pool whose springs are dried up and whose level rapidly sinks as soon as it is tapped at any point.

These brief hints must suffice to indicate the great importance of age among the predisposing causes of anæmia. At the same time they explain the clinical differences of susceptibility displayed by the organism at different epochs to noxæ which operate in different ways.

The greater activity of the nutritive processes in childhood is chiefly inferred from the ratio between the body-weight and the quantity of the principal excreta. The child and growing youth give off more carbonic acid and urea (relatively to the body-weight) in equal intervals of time than the adult. The evidence as regards urea may be found in the papers of Lecanu, Scherer, Bischoff, and Mosler; as regards carbonic acid, it is derived from the experiments of Scharling (see Bibliography, p. 282). Scherer gives 1.9 : 1 as the ratio between the production of urea in children and in adults. The ratio for carbonic acid, according to Scharling, is about 1.88 : 1. As regards these two ultimate products, therefore, which furnish the best criterion of the rate at which nutritive changes are going on, the figures are nearly twice as high in the child as in the adult. The few data we possess concerning the urine in old age (v. Bibra, Geist) tend to show that its absolute amount is markedly diminished. The quantity of urea is also lessened, though not to the same extent. As regards carbonic acid, the experiments of Andral and Gavarret point to a gradual decrease in its amount from about the fortieth year of life; so that the ratio between the proportion of the gas given off at forty and that given off at eighty may be approximately stated as 5 : 4.

The relative magnitude of the in-take in childhood and in adult life shows a still greater contrast than that of the out-put, for youth has not merely to cover its expenditure, but to provide for the growth of the organism. To this point we shall have to return when we come to speak of the prophylaxis of anæmia.

3. *Constitution.*—Within the somewhat arbitrary limits of health, we find that individuals differ in the degree of their pre-

disposition to anæmia, independently both of their age and sex. Such differences are intimately bound up with the physiological type of the individual constitution.

The term "constitution" has already been defined in my introductory observations (p. 252), but it may be well to remind the reader that the terms employed in this department of physiology, notwithstanding its pre-eminent theoretic and practical importance, are far from being precise. We have no accurate information concerning the differences that undoubtedly exist between the mechanism of the vital processes in different individuals. Accordingly, when at the bedside we speak in the traditional way about "strong," "weak," "relaxed," "plethoric," etc., constitutions, our phraseology expresses the results of our immediate intuition and subjective interpretation of the phenomena presented by the outward habit of the person examined, rather than any clear ideas about the true mechanism of the vital processes, such as could only be obtained by more exact methods of research. The indistinctness of our ideas entails an arbitrary employment of terms, and the latter, in its turn, reacts upon the former and adds to the obscurity of the subject. It is difficult to get anything consistent and precise out of this tangle of confused ideas and vague terms. We must limit our attempts in this direction to our immediate object, viz., the discovery and recognition of the predisposing causes of anæmia.

In the first place it is important to notice that the blood store differs in magnitude in different persons, all of whom may nevertheless be called "healthy" in the ordinary sense of the word; and that such differences are independent both of age and sex. Of course, the volume of blood cannot be determined during life, and we seldom have a chance of learning its centesimal composition in any particular case by direct analysis; still, the fullness of the vascular system, as inferred from the state of the pulse and the color of visible parts—further, the development of the muscular system and of the *panniculus*—furnish signs that enable us to judge of the amount of blood and of its functional value in any individual case. First, then, we have an unequal quantity of blood in different persons, an inequality which may be estimated at any rate approximately; next, we have differences in the state of bodily nutrition; and on these two sets of phenomena taken together we are able to found our primary division of healthy constitutions into such as are vigorous (rich in blood) and such as are feeble (spanæmic). It is self-evident that the predisposition of the latter to pathological oligæmia must be vastly greater than that of the former—nay, that the spanæmic constitution, as I have previously had occasion to remark, passes by insensible gradations into positive anæmia.

This tendency of feeble constitutions to positive anæmia is primarily general, equally susceptible of being heightened by such exciting causes as increase the consumption, or interfere with the renewal of the nutrient fluid; the lessened blood store, *per se*, entailing a predisposition to anæmia, just as it is partly to blame for the impaired nutrition of the tissues.

If, on the one hand, the mass or quantity of the available pabulum in the blood is in causal connection with the predisposition to anæmia, so also, on the other hand, is the rate at which the nutritive processes go on; indeed, this is one of the factors on which the amount of the blood store depends. The old school had a just notion of important constitutional differences, without, of course, having any clear insight into the individual factors concerned, when they spoke, *e. g.*, of relaxation or torpor, associating these terms with an idea of sluggish languor in the vital processes. The "relaxed" type of constitution is a very common one; and even when not already affected by definite disease, it is predisposed to anæmia, owing to its inability to resist consuming influences. Such constitutions resemble old age, and in some degree anticipate it by exhibiting during youth and manhood a relatively feeble power of renewing the functionally important elements of the blood. Hence, they usually continue to present an appearance of health so long only as no great claims are made upon the blood. The opposite of the "relaxed" type may be denoted by the term "tough"; "tone" may be taken as the opposite of "torpor." A "tough" or "tonic" constitution will thus denote one which possesses in a relatively high degree the power of rapidly supplying whatever losses the blood may undergo, by adequate exertions on the part of the chylopoëtic and cytogenic viscera, and which therefore enjoys a comparative degree of immunity from the effects of noxæ operating by way of consumption. Nutrition consists essentially, as I shall have to repeat again and again, in a physiological reciprocity between the blood and the tissues. The tissues play an *active* part in the nutritive process; they are consumers of the nutrient fluid; they are not merely nourished by it—they devour it. It is plain that the rate of molecular movement in the process of nutrition must depend, not merely on the rate at which the blood renews itself, but also on the rate at which it is consumed—in other words, on the appetite of the tissue-elements for food. There can be no doubt that such physiological diversities of corpuscular appetite really exist. The term "erethism" may fairly be borrowed from the older medicine to denote a state of the tissue-elements in which their desire for pabulum is relatively great. This state does not involve any predisposition to anæmia, so long as it is accompanied by an adequate energy of sanguification. On the contrary, the most healthy type of constitution is that which may be likened to an abundant stream with a considerable fall, *i. e.*, that which produces blood in abundance—thereby having a large store on which to draw—and also consumes it freely. This is not surprising when we reflect that some part of the energy which contributes to maintain nutrition is derived from the chemical affinities between the blood and the tissues. A large supply of blood, when of normal composition, must augment the activity of the nutritive process, both in extent and in intensity; just as, *cæteris paribus*, the rate at which a river flows is proportionate to the depth of the water in its bed.

But this "nutritive erethism" of the tissues, when strongly marked, may under certain conditions tend to increase the predisposition to anæmia, particularly if sanguification is unable to keep pace with it. Under such circumstances there arises a constitutional state which may be likened to a mountain torrent, poor in water but with a great fall—a state in which no reserve store can be accumulated, because the rapid consumption of material is only just covered by its renewal. In contrast to the "simple relaxation" analyzed above, such constitutions may be included under the head of "irritable weakness." Indeed, from the point of view of cellular pathology, it seems quite fair to extend the terms "erethism" and "irritability" from the *functional* aspect of cell-life to its trophic and plastic manifestations. It is clear that the condition of "irritable weakness" will chiefly show itself by increasing the susceptibility of the constitution to such noxæ as interfere with the renewal of the blood—to such as operate by way of inanition. Persons of this constitution are singularly incapable of resisting privations. Sometimes, however, under more favorable nutritive conditions (herein resembling, as already pointed out, the scanty torrent with its great fall), they may be capable of an amazing display of energy.

There is yet another form of constitution to be alluded to—that in which the power of renewing the constituents of the blood is unimpaired while the "nutritive erethism" of the tissues is relatively feeble. A superfluity of pabulum will thus accumulate in the blood, its conversion into tissue being delayed owing to the languor of the tissue elements themselves. The "plethora" induced in this way confers a certain immunity towards the ordinary causes of anæmia; but it does more than this. Persons of plethoric habit are often actually benefited, though only for a time, by exposure to influences which ordinarily induce slight anæmia, *e. g.*, the milder forms of fever.

A further question which connects itself with the above considerations is that of the objective signs by which the constitutional differences in question may be recognized. It would be idle to deny that no such certain criteria as those by which we estimate the total amount of the blood and the state of bodily nutrition [*i. e.*, the *level* of molecular movement in the system] exist for judging of the rate at which nutrition is going on, or, at any rate, that the most trustworthy signs are not as a rule such as arouse the attention of the physician. In most cases our only clue for tracing out at the bedside those differences of temperament which depend on variations in the rate at which nutrition goes on, is furnished *ex nocentibus*, *e. g.*, we infer that the patient is of a "relaxed" constitution where we find him unusually prone to succumb to such influences as promote consumption; we infer "irritable weakness" when he is prematurely exhausted by comparatively slight privations, and so on. Still, we do get some information from diversities of the habit, though such information is only of a conditional kind. Without going too far into details, I may point out in the first place that the "vigorous" or "robust" type of constitution, which unites the attribute of "toughness" to a certain measure of "nutritive erethism," is usually characterized by a full, strong pulse, a ruddy complexion, well-developed bones and muscles, together with a moderate layer of subcutaneous fat. Any more considerable development of the *panniculus adiposus* (especially when out of proportion with that of other structures), combined with the characters just enumerated, indicates what we have termed the "plethoric" type. The majority of fat and pasty people do not, however, belong to this category, but rather to the weakly, anæmic forms of constitution (for details, see the section on the Etiology of Obesity). They represent a state of organization in which the blood store is relatively small, and in which the nutritive processes, more especially, are relaxed and sluggish. A "relaxed anæmic" constitution is still more common without obesity. We then find the individual—his skeleton, and more especially his muscular system and *panniculus*—wearing an impoverished aspect. The defect of nutrition shows itself in the muscles—which are not masked, as they are in pasty people, by a thick layer of fat—whose nutritive tension (Virchow[1]) is relatively low, whose tonus is imperfect. We see this at a glance, and find the locomotive organs proportionately feeble. This form of habit occurring in persons whose constitution belongs to the relaxed anæmic type is closely allied to that in pathological anæmia; the former, indeed, passes into the latter quite as often as it follows it. Finally, as regards the aspect of persons with "irritable weakness" of nutrition, it may be stated broadly that in them the adipose tissue is reduced to its physiological minimum; they look lean, often quite withered. The muscular system, though sparingly developed, is not devoid of a certain degree of "nutritive tonus." In any case it is more capable of doing work than it is in the foregoing type of constitution, though, of course, it lacks the staying qualities exhibited by the muscles of the robust. Finally, the relative amount of the excreta, more especially of urea, would be of the utmost value as a measure of the rate at which the nutritive processes go on in the various types of constitution; for, taking the body weight, the accumulated fat of the *panniculus*, the degree of development, etc., into account, it would furnish the most reliable test of the activity of the nutritive processes going on in different healthy individuals. Unfortunately, this field of investigation is still all but uncultivated. The physician would have to subject his patients to systematic investigation, and to study their peculiarities when they are in health; but, if this were done in a sufficient number of cases, it would certainly do more than can be done in any other way to clear up our ideas on the subject.

I must say a few words about the causes to which the above diversities of constitution are due—so far as these causes are known, and so far as they have any bearing on the subject of anæmia. First, I may refer the reader to the observations made above (p. 267); I may remind him that the constitution of the individual is a result, partly of inheritance, partly of the operation of outward influences during fœtal and extra-uterine life. Thus, for example, that form of weakly constitution without actual disease which—now in the form of "relaxation," now in that of "irritable weakness"—is met with in so many persons, and so often passes into pathological anæmia, is often inherited from the male or the female parent, or from both of them together. A predisposition to oligæmia is often a family characteristic. Looking more deeply into the matter, we find this to mean that the average power of renewing the constituents of the blood, the average rapidity with which they are used up in nutrition and growth, and finally the average amount of the blood store (as the resultant of the first two elements), are collectively subject to hereditary influences. Hence, the exaggeration of constitutional weakliness into pathological anæmia may be a probability from the first. But, apart from this, the inherited type of constitution is susceptible of being considerably modified by outward causes; the tendency to anæmia may be augmented by changes in the environment. These outward causes are throughout identical with those which, when more intense, produce pathological oligæmia directly. They need not be enumerated here, since they will be fully discussed in the ensuing section, devoted to the exciting causes of anæmia.

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[1] Cellularpathologie. IV. Aufl. (1871.) p. 369.

Exciting Causes.

Whether there be any individual predisposition to anæmia or no, the disease may take one of two forms: it may arise as an independent malady—*idiopathic* anæmia—or as a consequence of some other morbid process—*symptomatic* anæmia. Before going on to consider the various disorders that may induce symptomatic anæmia, we shall consider those noxæ which are able to generate its idiopathic form.

1. *Deficient Supply of Food.*

Want and poverty, ignorance, malice, avarice, are often to blame for insufficient nourishment, and the anæmia and marasmus that result from it. So far as these cases of anæmia from inanition (using the word in its primary sense) come under medical observation and treatment, they are usually due to insufficient feeding, not to absolute starvation. The way in which anæmia results from defective feeding—defective either in quantity or in quality—is, upon the whole, plain enough to render any elaborate explanations superfluous; still, it may be as well to recall the following points succinctly to the reader's mind.

Inasmuch as cell-growth and nutrition involve a perpetual consumption of nutrient and plastic blood constituents, especially albuminates, and as the assimilative activity of the tissue elements is one of their *vital* properties, and therefore coeval with the life of each particular cell, it is clear that any reduction in the supply of nutriment from without must sooner or later diminish the total store of pabulum in the blood. Should the deficit be large, symptoms of anæmia make their appearance; they must be viewed not merely as the direct expression of the blood-change that has occurred, but also as effects of this blood-change on nutrition. For, although the trophic and plastic functions of the tissue elements are independent—*in kind*—of the supply of food to the body and of the magnitude of the blood store, still they are much influenced—*in degree*—by the state of the blood; they grow decidedly weaker when the latter is impaired. Hence, blood and tissues will suffer want, anæmia and marasmus will inevitably set in, whenever the supply of trophic and plastic material (albumen) continues to fall short for any length of time of the average physiological demand. The latter, of course, varies with the age, sex, constitution, etc., of the individual, and "insufficient food" is therefore a relative, not an absolute expression. (See section on *Predisposing Causes.*)

Inasmuch, moreover, as the mean nutrient value of the blood and the adequacy of the nutritive process depend primarily on the total amount of albumen assimilated in a given time, and in a much smaller degree on the mode in which its assimilation is distributed over that time, the symptoms of anæmia are equally prone to appear when the individual meals are all of them too restricted, and when the intervals between meals individually copious are too prolonged. In either case the supply of nourishment is insufficient to meet the physiological requirements of the organism; in either case alterations sooner or later set in, which, according to the degree of inanition and the idiosyncrasy of the affected subject, transgress the limits of health and culminate in actual disease.

It might appear, from the above remarks, as though a dietary poor in albuminous matter were pre-eminently fitted to induce anæmia. But our conception of insufficient nourishment must not be limited, as it has hitherto been purposely limited, to a deficient supply of albumen. Overwhelmingly important as albumen is for the organic processes of nutrition and growth, and certainly as anæmia and marasmus may be produced by undue restriction of the quantity of albumen in the diet, still we must not ignore the remaining constituents of what is known as a "mixed diet" in inquiring into the origin of anæmia from want of food. Physiology has shown, indeed, that the quantity of albumen required to maintain the blood in its normal state, and to preserve health, is largely dependent on that of other constituents of the dietary; and that the deficiency of albumen does not, of itself, enable us to estimate the degree of anæmia to be expected from insufficient feeding. The causal relation between want of food and anæmia must, therefore, be dealt with on wider and more inclusive principles. More especially ought we to take the physiological value of the other constituents of a mixed diet into account.

Considerations of space forbid me to go too far into detail. A few words are enough for the inorganic elements of food, the so-called "nutrient salts" (J. v. Liebig). These salts, like the albuminoids, are indispensable for the building up of the tissues. Any deficiency in their amount is inevitably followed by profound nutritive disturbances; but as these disturbances do not, strictly speaking, belong to the domain of anæmia, I cannot discuss them here.

Among the organic constituents of a mixed diet we have to consider (besides the albuminates), in the first place, fats; secondly, the so-called carbo-hydrates (sugar, gum, starch, etc.); thirdly, the so-called albuminoids (foremost among which stands gelatin). Their value as food, in the vulgar sense of the word, these substances owe, not so much to their directly nutritive and tissue-forming properties as to the ease with which they allow themselves to be split up and oxidized, thereby liberating energy. They supply the organism with the means of doing mechanical work and keeping up its temperature, and they also tend to economize the decomposition of the albuminates; for when they happen to be deficient, the albuminates are consumed in disproportionate amount, in order to supply energy for the most indispensable operations. It is chiefly in this way that the substances in question are of such immense, though indirect, importance to the strictly nutritive processes, and to the maintenance of the reserve of albumen in the blood. By undergoing decomposition they provide for the accomplishment of certain other essential and desirable functions of the organism, thereby hindering the oxidation and dissociation of the albuminates and allowing the latter to be reserved for the needs of growth and nutrition. In this wise they prevent a too rapid expenditure of the actually nutritive constituents of the blood (Bischoff, Pettenkofer, Voit, Fr. Hoffmann, et al.). Hence, a liberal supply of those substances enables the albumen simultaneously assimilated to accumulate in the blood; while, on the other hand, a deficient supply necessitates a more rapid consumption and decomposition of whatever albuminous compounds may be taken into the system, and may thus lead occasionally to a morbid degree of hypalbuminosis.

The lessened decomposition of albumen that results from an increased supply of fats, carbo-hydrates, and especially gelatin (Voit), may be inferred from the simultaneous changes in the amount of nitrogen excreted in the urine, fæces, etc. If to a uniform diet comprising albuminous matters, under which the body-weight remains constant, and there is equilibrium between the quantity of nitrogen taken in and the quantity cast out, we add a certain amount of the substances in question, a marked diminution speedily shows itself in the proportion of nitrogen eliminated. This diminution is roughly proportionate to the amount of fats, carbo-hydrates, etc., added to the albuminous constituents of the dietary, always supposing them to have been satisfactorily assimilated.

We thus see that the introduction of the substances in question into the dietary is by no means a matter of indifference. The blood is in greater danger of being impoverished when an inadequate supply of albumen coexists with an insufficient provision of the other constituents of a mixed diet, than when the albumen alone is deficient in amount. Indeed, we may go so far as to say that a man may escape anæmia even when the quantity of albumen in his food is relatively small, provided the lack of albumen is supplemented by an abundance of those other constituents; also that when a man's diet only contains just enough albumen to preserve his health, any diminution, whether of the albuminous or of the other constituents, will endanger his well-being.

The anæmia caused by imperfect alimentation is, accordingly, in the first instance a hypalbuminosis. In process of time, however, the blood shrinks in volume by losing a portion of its water; finally, the number of red corpuscles is invariably reduced. The lessened volume of the blood is a result of the colloid property of the albuminates, in virtue of which they imbibe water and fix a certain quantity of it more firmly in the blood; hence, when the proportion of albuminates is lessened, the nutrient fluid parts gradually with some of its water through the emunctory organs. The consecutive oligocythæmia, or reduction in the number of red corpuscles, on the other hand, is simply due to lessened production, owing to inadequate nourishment of the cytogenic organs; pathologically, therefore, it is on a par with the diminished energy of all the organic functions. When oligocythæmia has once become established as a result of insufficient alimentation, it may be expected, for reasons already given, to outlast the other alterations in the blood, *i. e.*, the diminution in volume and the hypalbuminosis. Again, we may anticipate, *à priori*, that in those forms of imperfect alimentation in which full meals are separated from one another by long intervals of complete or partial abstinence, the paroxysmal restitution of albuminates and water will render the persistent oligocythæmia the predominant alteration in the state of the blood. These, of course, are *à priori* conclusions, but they are fully confirmed by the results of experiments on the lower animals. Panum has succeeded in proving that partial starvation, enforced during repeated intervals or for a single long period, gives rise to a marked and excessive diminution in the proportion of colored elements in the blood.

All our accurate information concerning the alterations wrought in the composition of the blood by absolute starvation is derived from experiments on animals who have been starved to death. Such experiments have been made by Chossat, Bidder and Schmidt, Valentin, Heidenhain, Panum, Voit, and others, on various animals (pigeons, cats, dogs, etc.). We learn from them that, although the blood in absolute starvation undergoes, as might have been expected, a striking diminution in volume, yet this diminution is not out of proportion to that of the body as a whole. As regards the percentage composition of the blood, it has been found that, while the albuminates and salts of the plasma are diminished to a moderate extent, the proportion of red corpuscles is not appreciably altered. Accordingly, we may conclude that in absolute starvation it is only the solid constituents of the plasma that are reduced disproportionately, the total volume of the blood and the total quantity of red corpuscles being only reduced in proportion to the wasting of the remainder of the body (Panum). This proves, *inter alia*, that the red corpuscles, notwithstanding the shortness of their individual life, are, nevertheless, both consumed and renewed at a slower rate than the albuminates. Further, the comparatively small percentage diminution in amount of the albuminates renders it probable that during absolute starvation, in accordance with Voit's view, the so-called "organ albumen" is reconverted into the "circulating albumen" of the nutrient juices.

2. *Want of Light and Air.*

Persons deprived of fresh air and obliged to pass their time in close rooms (workshops, prisons, etc.) sooner or later begin to suffer from anæmia. Country people who migrate to a town suffer in the same way. On the other hand, it is well known that plenty of fresh air and a country life will invigorate an anæmic constitution, and that they are effectual elements in the treatment of the anæmic symptoms presented by convalescent patients. Further, it is commonly believed that, besides the want of fresh air, privation of sunlight will render even a strong constitution anæmic; hence the symptoms presented by those who work in mines, live in dark cellars, etc.—the pallid aspect of the proletary class in great cities and of a mining population.

It is not, indeed, unlikely that a prolonged lack of such beneficial vital stimuli as fresh air and sunshine should injure the general health and interfere with sanguification. More especially is there reason to believe (though no strict proof has yet been furnished) that the absence of those stimuli may interfere with the formation of red corpuscles, and thus give rise to a certain degree of oligocythæmia. But, so long as we have no exact observations to go upon, we need not attempt to define very precisely how those noxæ operate. We must not forget that persons deprived of light and air are usually subjected to other debilitating influences as well (especially want of food; excess or defect of bodily exercise, etc.), and that we can very seldom have an opportunity of watching the uncomplicated operation of the former set of causes.

3. *Excess or Defect of Bodily Exercise* (*Prolonged Repose, Fatigue*).

We know that a considerable amount of exercise is essential to the well-being of healthy persons, and that those who are debarred from it for any length of time, or who may indulge in physical laziness, become for the most part weakly and anæmic; the voluntary muscles grow flabby and finally waste in consequence of inactivity; fat accumulates in the areolar tissue; the previously healthy complexion assumes a pallid and earthy hue.

About the way in which this form of anæmia is brought about we can only say that it is probably by some interference with sanguification; increased consumption of the blood is clearly out of the question. The loss of appetite, that sooner or later results from protracted bodily inactivity, must unquestionably play a great part in producing the anæmia, for the reduced supply of nutrient matter is inevitably followed by hypalbuminosis, with its usual train of consequences. Further, deficient exercise may influence the digestive and cytogenic organs more directly, and thus interfere with sanguification; daily experience, at any rate, seems to show that, besides increasing the subjective demand for food, a certain amount of muscular activity quickens and perfects the actual process of digestion. Hence, we cannot be far wrong, notwithstanding our ignorance of the very complex mechanism concerned, in attributing the oligæmia produced by want of exercise to inanition.

But the very opposite condition, viz., prolonged over-exertion, likewise tends to injure the system. Exhausting bodily labor, especially when conjoined with want of food and other privations, is undoubtedly capable of bringing on anæmia. The term "hurtful over-exertion" is, however, relative; its meaning is not the same for all persons; no absolute maximum standard of allowable muscular work can be assigned. A tough (cf. p. 306) and vigorous constitution can go through very great and proonged exertion without injury, and do an amount of work that would be destructive to a person of frail and relaxed habit. Children, young persons not yet full grown, and old people, are more easily hurt by over-fatigue than vigorous adults in the prime of life. Again, we know that practice and habit may appreciably modify the individual standard of endurance. Lastly, it makes a great difference whether the exertion be continuous, lasting day and night, or interrupted by suitable ntervals of rest and sleep. In the latter case the constitution, especially when other circumstances are favorable, may continue to triumph for a long time.

There can be little doubt that the anæmia caused by over-exertion is of a consumptive character. For, in the first place, nothing promotes its actual origin and development more than simultaneous inanition from inadequate supply of nourishment. Nevertheless, the attempt to subordinate the pathological process to physiological laws, grounded, though it be, on common observation and experience, is not quite so easy as it might seem to be. The difficulties that have to be met, and how we may best meet them, will be made plain by the following considerations.

In any muscle that is doing work, molecular changes of two kinds are going on. In the first place, a muscle in a state of activity—as contrasted with one in repose—demands abundance of material from the blood for its *functional* renewal, that it may maintain its working power. Like every living tissue, it is able to attract to itself from the blood the material it requires—to exert a selective affinity. The losses to be repaired do not consist in albumen, for no albumen is decomposed in the act of contraction; they consist in oxygen, and in compounds of carbon with hydrogen. We must assume (L. Hermann) that muscle contains a store of a substance of complex chemical constitution (inogen, or energy-producing substance); during contraction this substance breaks up into an albuminoid body (myosin), which is retained in the muscle, and certain non-azotized products (carbonic acid, sarkolactic acid, glycerin-phosphoric acid, etc.), which are gradually removed by the circulating blood. Accordingly, for the maintenance of its functional powers, the muscular fibre requires non-azotized material (energy-producing material) only; and protracted muscular activity does not involve any increased consumption of the plasmatic albuminates for the functional renewal of the contractile tissue (Fick and Wislicenus, Voit, and others.)

But the muscle is not merely a machine for generating force; it is also a living tissue, that has to be maintained and nourished. This *nutritive* renewal of the muscular fibres demands for its accomplishment a constant supply of trophic and plastic blood constituents; it involves a perpetual consumption of albuminoid compounds, and this whether the muscle be active or at rest. Now, it is an interesting and important fact, first ascertained by Voit, that the formation of urea is not appreciably augmented by muscular work, and that the functional activity of a muscle is not attended by any considerably increased waste of its substance. Hence, it would appear to follow that, since the nutritive renewal, even of active muscle, does not involve any great consumption of the albumen of the blood, bodily over-exertion, severe fatigue, etc., cannot possess any special significance in the causation of anæmia, inasmuch as they do not give rise to any appreciable drain on the store of albumen in the blood.

Nevertheless, the actual state of things in protracted muscular exertion—in real fatigue—must be essentially different from what the above considerations would at first sight appear to indicate. It is quite true that the red corpuscles and plasmatic albuminates are by far the most important, because indispensable, constituents of the circulating fluid; still, the physiological value of the blood depends likewise upon its wealth in non-azotized energy-yielding matter. Now, since the latter is undeniably diminished during prolonged muscular activity, especially when (as in children, old and weakly persons) its original amount is below the normal average, or when, owing to such debilitating influences as want of food, etc., it is not renewed as fast as it is wanted, its one-sided diversion to the maintenance of muscular activity must necessarily interfere with other functions which are also dependent upon it for their supply of energy. By extending our conception of spanæmia we shall readily perceive that the poorness of the blood in energy-yielding material, resulting from extreme fatigue, must give rise to certain pathological phenomena which, from a clinical point of view, must be inseparably associated with the aggregate of symptoms that characterize anæmia. It is clear, moreover, that the activity of the muscular system will be the first to suffer when the store of energy-yielding material in the blood runs short.

But even the possibility of actual hypalbuminosis is not by any means excluded; quite the contrary. The excretion of urea during muscular over-work, though not largely, is undoubtedly increased (Voit, Heaton, Parkes, and others). Compare the following figures given by Voit:

A dog in a state of nitrogen equilibrium was found by Voit to be excreting 109 to 110 grammes of urea daily while at rest. On one occasion, however, the daily amount rose to 117 grammes, when the animal had been made to do 150,000 kilogrammètres of work by running for one hour on a tread-mill. On another occasion, it rose to 114 grammes, after the same amount of work had been done before the animal was fed. Lastly, the same animal, after nine days' starvation, was found to excrete 10.9 grammes of urea when at rest, 12.3 grammes when compelled to do work.

Ranke, in a course of experiments performed upon himself, observed a slight increase in the amount of urea eliminated during and particularly after active exercise. The increase (just as in Voit's experiments on animals) was far too slight to furnish any support to the notion that the muscular work accomplished was in any way dependent on the amount of albumen decomposed.

However slightly the formation of urea may be increased by exercise, still the summation of a long series of small deficits during continued over-exertion may easily come to amount to an appreciable drain on the store of albumen in the organism. *Gutta cavat lapidem, non vi, sed sæpe cadendo.* The hypalbuminosis thus induced will obviously be promoted by any cause tending to reduce the supply of albuminoids in the food—by the union of starvation with over-exertion. The truth of this *à priori* anticipation is amply confirmed by experience.

I may here allude to the interesting fact that muscles in a state of activity (as opposed to one of rest) do not merely maintain their *status quo*, but usually become hypertrophied, especially when the work they do is at all considerable. This must involve an increased withdrawal of true pabulum, *i. e.*, of albuminates from the blood; and these are not decomposed, but accumulate in the muscular tissue. Further, the muscle when once it is hypertrophied requires more albumen to keep up its nutrition than it did before. During protracted muscular exertion, accordingly, a larger proportion of the albumen of the blood is withdrawn from this fluid and diverted to the muscular system. Moreover, although the increased assimilation of albumen by muscles in a state of activity undoubtedly goes on more quickly when the supply of food is abundant, yet the cellular activity of the muscular fibres is in a certain measure independent of the dietary. Should the store of albumen in the blood be insufficient from the first, or should a man who is obliged to continue at work be suddenly deprived of food, the development of hypalbuminosis will certainly be promoted by the requisition made by the muscles on the blood. These remarks will suffice for the present to render the production of anæmia by over-exertion in some degree intelligible.

4. *Unusual States of Temperature.* (Influence of Heat and Cold.)

Season, weather, and climate, with their attendant changes of atmospheric temperature, appear to influence the development of oligæmia. Experience teaches us that extremes of heat and cold exert a weakening influence upon the system. This influence is felt most severely by those who have been used to medium temperatures only, and who are unable to adopt suitable measures for their protection. Now, although the ultimate result—the development of anæmia—is the same under either extreme of temperature, still the way in which it is reached is very different, in all likelihood absolutely opposite, in the two cases.

The influence of prolonged and excessive heat in bringing on anæmia is better known and more certainly established than that of cold. It is principally exemplified in Europeans, who have emigrated to a hot climate and have been exposed for some length of time to its effects. Apart from certain special forms of anæmia common in hot countries (malarial anæmia, anchylostoma disease), there remain a vast number of cases in which the poorness of the blood must be attributed directly to the heat—cases of "tropical anæmia." In the mode of its occurrence this disorder simulates that form of anæmia which develops itself in the temperate zone as a result of insufficient exercise, and which has already been described. The patient's vigorous appetite gradually begins to fail; he is overpowered by an overwhelming languor; his complexion grows pallid; finally he begins to lose flesh, his nutrition becomes impaired. The disinclination for exercise, the longing for repose, which speedily lay hold of the new-comer, undoubtedly contribute in some measure to bring on tropical anæmia. Many persons give themselves up completely to a *far niente* state, and this, in its turn, tends to weaken them. But it would be a mistake to deny the directly injurious effects of a high external temperature upon the blood. For the exhausting influence of a hot climate is too great to be accounted for by mere bodily inactivity; moreover, it manifests itself in an uncomplicated form in such persons as are obliged, by the nature of their avocations, to lead an active life. We must regard the climate itself as the chief factor in the production of tropical anæmia, and ascribe the main share in the result to the prolonged heat. Lastly, we must not shut our eyes to the fact that even in the temperate zone, an unusually hot summer produces manifest anæmia in many persons, especially women and children—an anæmia similar in kind to that observed in the tropics, though differing from it in degree.

As regards its pathogeny, this form of anæmia probably starts from a disturbance of sanguification, just like the form which arises in consequence of want of exercise. In either form, loss of appetite and possibly direct enfeeblement of the digestive powers may be regarded as playing a prominent part; but as precise information on this point is still wanting, further speculation concerning it is undesirable.

The long cold of winter appears likewise to be capable, in the absence of due protection, of causing, or at any rate promoting the development of anæmia. Daily experience shows that the poor, who are scantily clad and obliged to live in unheated rooms, or possibly without a shelter at all, suffer more severely rom impaired nutrition in cold weather than during the summer months. So too, the exhausting effect of military service makes itself felt most forcibly during a winter campaign. Some light is thrown on the way in which a low external temperature operates by the fact that its hurtful effects are always aggravated by simultaneous insufficiency of food; whereas, if food be plentiful, they show themselves in a very minor degree or not at all. This, together with the fact that subjective hunger is always more intense in cold winter weather than in summer, renders it probable that the anæmia caused by cold is of the consumptive kind. When we reflect on the unfavorable conditions that surround so many of our poor in winter, and on the calamitous history of campaigns undertaken during the cold season, we are tempted to envy many of the lower animals the gift of hibernation they have acquired (or retained?), which enables these our favored brethren, when their supply of food runs short, to reduce their production of heat and carbonic acid to a minimum without perishing. Man is, unfortunately, otherwise situated. As Liebermeister formerly pointed out, and has recently proved by conclusive experiments, the effect of a low temperature on the surface of the human body is to *increase* the production of heat and carbonic acid. The effect of cold would thus appear to be like that of muscular exertion. We can now understand, in some measure, why it is that we can put up fairly with cold, provided we have food in abundance, whereas we are quickly exhausted by the combined operation of cold and hunger; also why our subjective craving for food should be greater in cold than in hot weather.

Liebermeister's original investigations enabled him to show that cold baths increased the production of heat. These investigations were conducted by calorimetric methods on a very large number of persons, and with a variety of experimental modifications. He has recently completed these calorimetric results by determining chemically the amount of carbonic acid given off. He finds the production of heat and the elimination of carbonic acid to increase *pari passu* with every reduction in the temperature of the ambient medium (whether air or water). Inasmuch, moreover, as the excretion of carbonic acid is not diminished during the period immediately succeeding immersion in cold water, but on the contrary remains high, it is plain that not merely the elimination, but the actual formation of carbonic acid is increased by cold—some of the excess of carbonic acid being excreted after the cold has ceased to act. Lastly, it was found that the intensity of these processes was different in different persons. For further details the reader is referred to Liebermeister's own papers, a list of which is given in the catalogue of works prefixed to the present chapter.

. *Increased Expenditure of Unoxidized Material.* (Physiological Discharges.)

The physiological expenditure of the human body consists hiefly of water (urine, sweat, exhalation from lungs and skin), nd of certain so-called ultimate products (carbonic acid, urea, ric acid, etc.) whose chemical composition shows them to be oor in potential energy, and, therefore, physiologically useless ompounds, resulting from the oxidation and dissociation of thers that are more complex and endowed with a larger store of nergy. Chemistry shows that most of these educts are inca-able of supplying energy or maintaining nutrition ; so that by his part of its expenditure the organism undergoes no physiolo-ical loss worth speaking of. But there are certain other forms f expenditure, of a more occasional kind, which entail the loss f substances rich in potential energy—substances containing uch albumen, fatty matter, and other complex and physiolo-ically valuable compounds. They are lost to the individual, ut normally destined to subserve the origin and nutrition of ther individuals. I refer to the seminal emissions of the male, nd the secretion of milk in the female.

The accomplishment of the sexual function with the attend-nt discharge of semen does not appear to weaken the constitu-on, when vigorous and healthy, provided always that it be xercised within the limits of discretion, that the supply of ourishment be adequate, and the assimilative powers intact. ut profuse discharges of semen in consequence of venereal xcess are quite capable of producing anæmia, especially if the dividual be of weakly habit and possess a meagre store of lood ; also, if any disturbance of sanguification happen to coin-de with the sexual excesses. The connection between cause d effect is clear enough when we consider that the generative ands separate a product rich in energy from the blood. Any sproportionate increase in the activity of those glands is inevi-bly followed by a marked diminution of the aggregate store of trient and energy-yielding substances in the blood ; and this ust lead to anæmia, unless the original store be relatively great, d the task of compensation be not interfered with.

The above considerations apply likewise, but with much greater force, to the lacteal secretion. The female organism, when healthy and vigorous, usually bears (supposing the mammary glands suited to fulfil their office during the appointed period) the drain of albuminoid matters (casein), fat, lactose, etc., very satisfactorily for a certain time, though the amount of unoxidized matter withdrawn from the blood during lactation is enormous. This, however, is only possible when an increased appetite for food, and an increased power of assimilating it, coexist with the increased expenditure. Should suckling be continued for an immoderate length of time, the appetite usually begins to fail, and symptoms of anæmia frequently appear even in strong women, warning them against a continuance of lactation. On the other hand, women who are not strong to begin with—whose blood-store is scanty—are often quite unable to bear the strain of nourishing their offspring, and quickly become anæmic if they attempt to fulfil their maternal duties. Lastly, lactation speedily becomes dangerous to the mother's well-being, when any accidental disturbance of digestion or other cause of weakness happens to associate itself with suckling. Accordingly, it is clear that venereal excesses in the male, and lactation in the female, do not always give rise to anæmia solely or even principally on account of the absolute quantity of matter withdrawn from the blood. Anæmia is not usually developed (putting aside extreme cases) until some additional predisposing or exciting cause comes into operation.

Menstruation, though a normal attribute of the female organism during the period of its sexual maturity, often serves as an auxiliary cause in the production of anæmia. I am not speaking of the pathological forms of profuse menorrhagia, which are naturally and almost invariably followed by symptomatic oligæmia; I allude to the normal loss of blood which occurs periodically in ordinary menstruation. Such losses are easily borne by healthy women; they are very prone, however, especially when they coexist with other depressing influences, to produce or to aggravate anæmia in women who are already out of health, and in young girls. It is an interesting fact that the menses are not arrested or even diminished in all cases of anæmia; neither does the amount of discharge in health correspond invariably to the state of individual nutrition and the presumable magnitude of the blood store. Should there be any marked degree of disproportion between them, symptoms of anæmia may be expected to arise during and after each menstrual period, lasting for a variable time according to the circumstances of the case. A special consideration of the changes which the blood undergoes in consequence of direct hemorrhage must be reserved for a subquent page (p. 326).

6. *Psychical Influences.*

Depressing emotions are commonly believed to do harm by weakening the constitution and engendering oligæmia. That care and grief "make the cheek grow pale" and "gnaw at our life and health," is sad truth, not mere poetic fiction. Nevertheless, although the effect of these emotions in producing anæmia is firmly established by simple observation, we are still ignorant of the way in which they act upon the blood. Direct investigation is needed before we can decide whether depressing emotions primarily interfere with sanguification, causing anæmia by way of inanition, or do really "gnaw" at the blood, *i. e.*, increase the consumption of its elements. Supposing the former of these views to be the correct one, we have to determine whether the anorexia so frequently associated with grief and anxiety is the chief cause of the oligæmia. It is quite possible that influences of either kind may co-operate in the impoverishment of the blood; these cases would then come under the category of "anæmia of complex origin" (p. 293).

The same may be said of the influence of mental over-work in causing anæmia, which is not, however, so conclusively established.

We may now pass on to another part of our subject, viz., the etiology of the symptomatic forms of oligæmia. We shall pass the more important of the morbid processes, during whose course anæmia has been observed to arise, in review.

By way of introduction, it may be laid down as a general law that nearly every morbid process, when it occurs in a severe form, is sooner or later followed by anæmia. Hence, the symptomatic varieties of anæmia, as regards their local origin, belong to the most divers categories of special pathology. It would obviously be impracticable to enumerate the latter one by one; we must limit ourselves to the enumeration of those general processes which are capable—irrespectively of the special localization of the primary mischief—of producing anæmia in virtue of their pathological character.

a. *Hemorrhage, External and Internal.*

I have already pointed out that menstruation, a physiological hemorrhage peculiar to the female sex, may under certain circumstances act as a cause of anæmia. This is true in a far higher degree of all the pathological varieties of direct hemorrhage, whether external or internal. Either of these may result from a multitude of causes, and may lead—according to the amount of blood lost, the rate at which it is poured out, and the previous magnitude of the blood-store—now to the milder, now to the more severe forms of oligæmia. The connection of the phenomena is so transparent that it would be superfluous to devote any further consideration to the pathogeny of these forms of anæmia. The following question, however, merits our attention: What are the special changes, as regards volume and centesimal composition, wrought in the blood, whether mediately (*i. e.*, subsequently), or immediately, by direct hemorrhage?

We might anticipate that the immediate effect of hemorrhage would exclusively consist in a diminution of the volume of the blood—an *oligæmia vera seu pura*, in the language of general pathology; likewise, that, after the bleeding had stopped, further changes—more particularly in the centesimal composition of the blood—would gradually be developed in a typical order of succession; for, even allowing that the *immediate* alteration in the blood deserves the name of an *oligæmia pura*, it is obvious, for reasons given above, that the gradual restoration of the individual constituents of the circulating fluid will not take place uniformly—that the *oligæmia pura* cannot possibly last long. Of a truth, we find from examination of the blood in persons who have recently suffered from hemorrhage, and from an analysis of the symptoms they continue to present, that, in harmony with physiological laws, the volume of the blood is quickly restored to its previous standard by the absorption of water, that the proportion of plasmatic albuminates remains abnormally low for some time longer, and that a still longer interval is requisite before the oligocythæmia can be entirely remedied.

But Vierordt showed long ago, by experiments on animals, that the blood actually exhibits definite changes in its centesimal composition, and not merely a diminution in its volume *immediately* after a profuse hemorrhage. By examining samples of blood taken immediately after venesection, he discovered that the blood is relatively poorer in albumen and red corpuscles, richer in water and leucocytes, even while the bleeding is going on, and in direct proportion to its amount. The increase in the number of leucocytes and the decrease in the number of red discs are very marked when the quantity of blood lost is considerable, and the immediate effect of a profuse hemorrhage does not, therefore, consist, as might have been expected, in an *oligœmia pura*, but in a complex dyscrasia made up of hypalbuminosis, leucocytosis, and oligocythæmia. The last-named alteration, like the hypalbuminosis, continues to increase for a time after the bleeding has stopped, and then gradually subsides.

These facts admit of a simple explanation, if we reflect that, even while the bleeding is going on, the blood-pressure in the arteries, capillaries, and veins is reduced, owing to the diminished volume of fluid contained in them. The decrease of intravascular tension speedily determines an acceleration of the flow of lymph and of the osmotic current of tissue-juices towards the blood. The afflux of lymph induces leucocytosis ; the tissue-juices, containing much water and little albumen, dilute the highly concentrated blood. Both of these processes go on, though with gradually diminishing intensity, for some time after the bleeding has ceased. The albumen of the blood is slowly restored by the introduction of nourishment, and the red corpuscles yet more slowly by the formation of new ones.

The annexed figures are borrowed from Vierordt's paper (loc. cit., p. 271). They exhibit very clearly the progressive diminution in the number of red corpuscles contained in samples of blood from one and the same animal (a dog), after repeated bleedings. To make the values comparable, the amount of blood lost is expressed in terms of the body-weight, while the proportion of red corpuscles in the successive samples is given in centesimal parts of the normal proportion, determined by direct enumeration, in a small sample of blood drawn before the commencement of the experiment.

Amount of blood lost expressed as a fraction of the body-weight.	Proportion of red corpuscles, expressed in hundredths of the normal proportion.
0	100
$\frac{1}{100}$	89
$\frac{1}{47}$	81
$\frac{1}{30}$	75
$\frac{1}{18}$	69
$\frac{1}{17}$	52
	(Death of the animal.)

Vierordt corroborates the observation previously made by Nasse, to the effect that the red corpuscles remaining in the vessels after profuse hemorrhage are visibly paler than usual. [Is this due to a larger admixture of young corpuscles which have not yet got their full color—which are still, in a sense, immature? Or ought it to be attributed to imbibition of water from the diluted plasma? The former is the more likely alternative, for the corpuscles are not altered in form.] The leucocytosis which follows copious hemorrhage is ascribed by some writers to the greater adhesiveness of the leucocytes, which makes them stick to the walls of the vessels, and thus interferes with their escape in the stream of blood! This explanation is extremely forced. It would make the apparent increase in the number of leucocytes purely relative. Moreover, it becomes superfluous if we adopt the view enunciated above—a view that is not open to any legitimate objection.

b. *Pathological Discharges.*

Genetically allied to the anæmia caused by hemorrhage is that form of the disorder which results from pathological discharges. The latter consist either of matters directly withdrawn from the blood, or of compounds destined for its renewal; the former are abstracted from the circulating fluid, the latter are not allowed to reach it.

The deleterious effect of pathological discharges on the blood is proportionate to their abundance and to the quantity of albuminoids or their derivatives which they contain. Since most of the processes included under this head involve an *indirect* expenditure of blood constituents, they are intimately related, as regards the way they induce anæmia, to the physiological discharges alluded to above (p. 323). Indeed, those physiological discharges may attain a pathological degree of significance in consequence of local mischief in the excreting organs. Then, of course, the resulting anæmia ceases to belong to the idiopathic category. Many cases of symptomatic anæmia, for example, may be traced in males to spermatorrhœa, in females to galactorrhœa; the former being primarily due to disease of the male generative organs (*vesiculæ seminales*), the latter to disease of the mammary glands. From our present point of view, however, the anæmia resulting from discharges which are *ab initio* pathological is of more importance. Suppose the urine, normally free from albumen, to contain it, owing to some affection of the kidneys. The albuminuria is strictly pathological. It soon leads, as a rule, to a pathological hypalbuminosis of the blood, and to this, owing to impaired nutrition, oligocythæmia, etc., are quickly superadded. Occasionally, too, blennorrhœal affections of certain mucous surfaces (the lining membrane of the respiratory passages, of the uropoëtic apparatus) produce similar results, the perverted and morbidly exaggerated secretion withdrawing large quantities of albumen, partly as such, partly in a derived form (mucin), from the organism and the blood. The same thing happens in dysentery of the large intestine, according to F. Oesterlen and C. Schmidt; the frequent occurrence of extreme hypalbuminosis in dysenteric patients—so extreme as to give rise to general dropsy—being readily explained by the quantity of albumen contained in dysenteric stools.

But anæmia may result from other forms of diarrhœa as well, and its pathogeny is not invariably the same. In dysentery the leading phenomenon is an abundant excretion of albumen from the blood, and the anæmia is chiefly brought to pass by way of consumption. In most other forms of diarrhœa, on the other hand, the primary phenomenon is of a different kind, *i. e.*, increased peristalsis of the small intestine (Traube, Radziewski, and others). The contents of the bowel are hurried along at an unusually rapid rate, and the chyme imperfectly assimilated. The more or less fluid motion furnishes the clearest proof of its origin by the quantity of peptones, fatty matter, etc., it contains. When anæmia is brought on by protracted diarrhœa of this kind, it must obviously be by way of inanition—the hungry blood is balked of the albuminates, fats, etc., needed for its renewal. Lastly, I have already pointed out, in the course of my introductory remarks to the present section, that choleraic diarrhœa, in which the discharges contain an abundance of water and but little albumen, gives rise to symptoms not so much of oligæmia as of over-concentration of the blood.

There still remain a certain number of discharges which induce anæmia by way of consumption. I have not yet alluded to them, inasmuch as they diverge farther from the physiological type of the secretory process than the instances just enumerated. None the less is the anæmia resulting from extensive suppuration or mortification of the tissues, or from the exudation of large quantities of liquid into the peritoneal, pleural, or pericardial cavities, or from large pneumonic infiltrations, etc., closely allied in its mode of origin to that form of the disorder which results from anomalies of secretion. It is largely due to the indirect losses experienced by the blood during the processes in question. It is true that in most cases other influences, especially the fever which is usually present, co-operate with the discharge to induce the anæmic state.

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Malignant Growths.

Certain local processes of proliferation, manifesting themselves in the form of tumors, are clinically defined as "malignant." This group includes the softer varieties of cancer and sarcoma which tend to recur after extirpation, to multiply and become generalized, and above all, to grow very rapidly, to be very rich in corpuscular elements, and to break down. It is true that the deleterious effect of these growths is often due, in great measure, to the metamorphosis and destruction of the parent tissue in which they originate, whose place they usurp, and whose functions (often essential to life) they sooner or later interrupt. But this result is *per se* mainly of an accidental kind, determined by the anatomical seat of the tumors, and would in nowise entitle us to attribute a malignant character to the new growth as such—to the products of proliferation. In marked contrast to this *accidental* malignity of many so-called malignant tumors—a malignity equally manifested by benign growths (lipomata, fibroids, etc.) occupying the same localities and attaining the same size—stands the *essential* malignity of the true malignant growths, which is wholly independent of their seat, results from their mere presence in the body, their mode of increase and subsequent disintegration, the way in which they spread, etc., and manifests itself by their deleterious effect upon the blood and the general nutrition of the body.

The severe and usually fatal cachexia that often shows itself in patients suffering from cancer and sarcoma, with the symptoms of extreme anæmia and marasmus, is frequently due, in no small degree, to the tendency of the growth to soften and the profuse drain thereby set up. But the anæmia and marasmus often make their appearance long before disintegration has begun; nay, many patients succumb to exhaustion before their tumors show any sign of softening. Accordingly, there must be other reasons for their malignant properties. Their destructive influence upon the blood may partly be accounted for by the rapidity of their growth, the number of corpuscular elements they contain, their almost invariable tendency to recur in their original situation, their proneness to become generalized. That destructive influence consists undoubtedly in a continual drain upon the nutrient resources of the blood. The blood is robbed at the expense of the healthy tissues, which are starved and languish. These parasites, endowed with a morbid quickness of growth, may be likened to those succulent annuals (pumpkin, sun-flower) which impoverish the soil and unfit it for supporting other vegetation. They also resemble weeds which can hardly be eradicated, which spread in all directions, amid whose luxuriance the cultivated plants pine for want of the nourishment they need.

Comparisons of this kind may help us to realize the essential malignity of pseudoplastic formations in a general way; but there remains the possibility that, besides the properties I have enumerated, there may be others concerning which we are ignorant, promoting the development of the cachexia. Poisonous fluids may be secreted by these juicy tumors and poured into the blood. Pathologists are already inclined to admit that they may possess a certain local infective power (Virchow). But these and similar speculations are still in want of proof; hence, a critical examination of them would be out of place in a hand-book like the present.

d. *Toxic and Infective Processes.*

Many poisons cause anæmia by decomposing the albuminates of the plasma, dissolving the red corpuscles, etc., when they have entered the circulation. Accordingly, the blood undergoes changes which may be collectively designated as "toxic or infective anæmia." I need only allude to the so-called "malarial anæmia" (malarial chlorosis), to poisoning by the mineral acids, phosphorus, and other substances, and refer the reader for further information to other volumes of the present work, specially devoted to infective disorders and poisons.

e. *Animal Parasites.*

Certain forms of anæmia are caused by the presence of animal parasites in the body (especially in the alimentary canal), owing to the greedy way in which many of these unbidden guests abuse the hospitality of their entertainer. I need only refer by way of illustration (*see* Vol. III., Vol. VII.) to the notorious "tropical chlorosis" (*Cachexia africana s. americana, ægyptiaca; hypoæmia intertropicalis; geophagia s. allotriophagia*). This variety of oligæmia is due to the entrance of certain blood-sucking entozoa (*anchylostomum duodenale*) into the patient's alimentary canal. Griesinger was the first to point out the causal connection between a severe form of endemic anæmia he observed in Egypt, and the presence of these parasites in the duodenum. He established the facts by post-mortem examination. Other observers have since confirmed his interesting discovery (Pruner, Bilharz, Wucherer, Moura, Tourinho, Monestier, Grenet, Rion Kérangel) and extended it to other countries as well (Brazil, Cayenne, Comoro Islands)

f. *Obstacles to taking Food.*

Symptomatic anæmia caused by obstacles to the ingestion of food is etiologically contrasted with idiopathic anæmia caused by want of food; but the changes which the blood undergoes are, of course, the same in both. It will, therefore, be sufficient to enumerate the morbid processes that come under this head, and refer to the observations on p. 311 for an account of the way in which they operate. Foremost among them stand all such diseases of the mouth, pharynx, œsophagus, and cardia which interfere with or prevent the prehension, mastication, and deglutition of food; also maladies attended by obstinate or uncontrollable vomiting. Vomiting is not confined to disorders of the digestive system; it is quite as frequently due to other causes (*e. g.*, acute and chronic uræmia, cerebral disease, pregnancy, etc.). Hence the manifold diversity of the causes by which this form of symptomatic anæmia may be brought on.

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g. *Dyspepsia.*

Dyspepsia, including under this term all disturbances in the chemistry of digestion, is a more frequent cause of anæmia than obstacles to the ingestion of food. Anomalies of secretion, owing to which the peptic action of the gastric juice, succus entericus, pancreatic fluid, and bile is interfered with, occur not only in connection with coarse structural lesions of the stomach, intestines, pancreas, and liver, but are likewise associated with less definite disturbances in the nutrition of these parts. Often, moreover, they seem to result from disordered innervation of the digestive glands, from local or general disturbances of the circulation, from changes in the composition of the blood. The causes of dyspepsia, and therefore of the consequent anæmia, are thus seen to be manifold; I need only allude to a few by way of illustration. Our first attention is claimed by acute and chronic catarrhal affections of the stomach and intestines; for they are extremely common, and often cause both mild and severe anæmia. Next comes the dyspepsia due to psychical influences (sorrow, anxiety, worry, etc.)—nervous dyspepsia. As instances of circulatory troubles interfering with digestion, we have the cases in which fluid effusions into the peritoneal cavity, abdominal tumors, etc., hinder the secretory activity of the glandular organs subservient to digestion by mechanical pressure upon the vessels. Lastly, the so-called "atonic dyspepsia" of anæmic persons is an instructive example of the origin of dyspepsia from alterations in the composition of the blood. For the anæmia is here the immediate cause of the dyspepsia by which it is, in turn, exaggerated. For since every variety of anæmia, whatever be its cause, lessens the secretion of peptic juices, it must hinder the assimilation of nourishment and thus intensify itself by way of inanition. When I come to speak of treatment I shall have to point out how this vicious circle, in which so many patients are unluckily involved, may be most easily escaped from.

Dyspepsia inflicts a twofold injury upon the blood and the organism. In the first place, the blood fails to receive an adequate supply of material for the renewal of constituents essential to the adequate fulfilment of its functions; the organism is thus *directly* exposed to the risk of inanition. Secondly, there is the danger that when any considerable amount of food has been introduced into the alimentary canal, a portion of it will remain undigested, will undergo abnormal chemical changes, and irritate the mucous lining of the stomach and intestines. The secondary catarrh thus induced will react upon the dyspepsia and make it worse; thus we get another vicious circle, somewhat different from that described above, but which, to judge from the symptoms, is not less common.

The anæmia that results from dyspepsia consists primarily, as might be expected, in a hypalbuminosis. If the assimilation of fats and carbo-hydrates be simultaneously interfered with, the non-nitrogenous constituents of the blood will run short likewise; this, too, will react unfavorably on the store of albumen (cf. p. 313). In any case, the total amount of nutrient and plastic material in the blood will be more or less considerably reduced, and the consequent inanition will retard the formation of new red corpuscles. In short, the phenomena will obey the same laws as in anæmia from want of food or from hindrances to its ingestion.

h. *Venous Stasis.*

Cardiac and pulmonary diseases that are attended by passive congestion usually lead, sooner or later, to changes in the composition of the blood: first, by the impediment offered to the entrance of lymph and chyle into the circulation by the distended state of the systemic veins; secondly, by the catarrh of the gastro-intestinal surface, which usually results from venous hyperæmia; the catarrh causes dyspepsia, and thus interferes with the absorption of nutriment (cf. section "g"); lastly, should dropsy come on, the transudation of highly albuminous liquid will further promote the development of anæmia, or, at any rate, of hypalbuminosis. Thus it is that patients afflicted with such maladies almost invariably present symptoms of anæmia and impaired nutrition in addition to those which result directly from the circulatory disturbance. Accordingly, Andral, Gendrin, and other French authors are perfectly right in viewing a disordered circulation as a frequent cause of anæmia, and in speaking of a "cachéxie cardiaque," or general cachexia of patients suffering from heart-disease.

i. *Impaired Sanguification from Disease of the Cytogenic Organs* (*Spleen*, *Lymphatic Glands*, *Medulla of the Bones*, *etc.*)

Since it is highly probable that the red corpuscles are produced by a gradual metamorphosis of corpuscular elements derived from the so-called cytogenic organs, especially the spleen, lymphatic glands, and marrow of the bones, it is clear that a state of anæmia—more strictly, of oligocythæmia—may be induced, either when these corpuscular elements are not formed in sufficient quantity, or when their metamorphosis does not follow its normal course, or lastly, when they are retained in the cytogenic organs. Every one of these possibilities appears to be occasionally realized; though the precise mode in which the individual forms of anæmia belonging to this group arise has not yet been thoroughly established.

A defective production of red corpuscles is probably associated with all states of impaired nutrition or marasmus. In such cases it must be viewed, not as the primary cause of the anæmia, but as the result of a primary hypalbuminosis. Gradually, however, it assumes more and more importance, and serves to complete the symptoms of anæmia by adding oligocythæmia to hypalbuminosis. On the other hand, that form of oligocythæmia which we term chlorosis must be regarded as essentially a disorder of sanguification. It will be fully discussed in the next chapter. We assume that it depends on a diminished formation or hypoplasia of those protoblasts from which the red corpuscles are developed. The various forms of leukhæmia, on the other hand (splenic, lymphatic, myelogenic), present us with a different state of things; the protoblasts are formed in immense numbers in the cytogenic organs, but their further development is arrested (*i. e.*, they degenerate into multinuclear leucocytes); and this is the essential feature in the morbid process—that which exerts an injurious influence upon the blood. Lastly, there are those cases of anæmia—almost invariably fatal, though luckily not common—associated with enlargement of the spleen and lymphatic glands, and known as "splenic anæmia," "lymphatic anæmia," "pseudoleukhæmia" (Hodgkin's disease, multiple pernicious adénie, malignant multiple lymphosarcoma, malignant lymphoma, multiple dermoid carcinoma, etc.). These are chiefly due to retention of the corpuscular elements in the cytogenic organs (see Vol. VIII.). It is quite possible that such retention may likewise play a certain, though by no means the sole part in the causation of many forms of anæmia and enlargement of lymphatic glands occurring in scrofulous, syphilitic, and other conditions. These morbid processes are all fully described in other volumes of the present work; it is enough for me to point out that there are various ways in which anæmia may be connected with diseases of the spleen and lymphatic glands.

k. *Fever.*

Among the numerous pathological processes during which anæmia is developed, fever must be included. Fever will be the last, but not by any means the least, important member of that series of causes which we have been considering. True, the febrile process is not one of the most frequent causes of anæmia, but the form of anæmia which it provokes—febrile anæmia—is distinguished from most of its congeners by the relative rapidity of its development. In this respect it is only excelled by direct loss of blood—profuse hemorrhage; and it is worthy of note that the attendant marasmus is neither so intense nor so speedy in making its appearance, after even abundant hemorrhage, as it is in fever (cf. Symptomatology). As Virchow[1] justly pointed out a long while ago, every kind of fever is really endowed with hectic properties; and it may be said generally "that anæmia and marasmus arise in the course of the febrile process with a rapidity and intensity proportionate to the severity and duration of pyrexia" (Liebermeister[2]).

The pathogeny of febrile oligæmia and of the marasmus associated with it is complex. Divers factors co-operate to produce them, and they work in divers ways. As regards the latter point, we know that on the one hand almost all febrile patients are in a state of marked inanition, which must exert a great influence on the state of the blood, and indirectly on the nutrition of the body as a whole; on the other hand, the consumption of the blood constituents and the tissues is abnormally quickened; so that, even for the mere maintenance of the blood and tissues *in statu quo*, the conditions, during fever, are the most unfavorable that can be conceived. These facts, roughly as I have sketched them, are sufficient to account for the rapidity with which anæmia and marasmus are induced by fever, and for their reaching so extreme a degree of intensity when the fever has lasted for any time.

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[1] Handbuch der spec. Pathol. und Therapie. I. (1854) p. 37.

[2] Prager Vierteljahrschrift. LXXXVII. p. 1 et seq.

This is no place for discussing the prevailing theories concerning fever, or examining the controverted points in this important region of pathology. It will suffice for our purpose briefly to enumerate a series of facts which may now be regarded as established, and whose bearing upon the subject in hand is obvious.

The state of inanition in a febrile patient is, in the first place, greatly promoted by the loss of appetite usually present, and perhaps never absent when the fever is at all high. Moreover, the febrile process, when severe, is attended by more or less disturbance of digestion, which may hinder or altogether prevent the assimilation of any considerable amount of nourishment. It has long been known, for instance, that the secretion of gastric juice is much impaired in the febrile state (Beaumont). The same is true (to judge from the symptoms) of the pancreatic secretion and succus entericus. Hence it is that febrile patients digest extremely little albumen, and, as a rule, but little fatty matter also ; the digestion of carbo-hydrates seems to be less interfered with. Under such circumstances, the renewal of the albumen of the blood must be very imperfect, as also that of the non-azotized energy-yielding material ; and the nutrition and functional activity of all the organs must suffer in consequence. Further, we may confidently assume that the formation of red corpuscles will be checked, and that the symptoms of oligocythæmia manifested by febrile patients must, at any rate in some degree, be ascribed to the existing state of inanition.

But the increased consumption that takes place in fever is not of less importance than the inanition ; nay, its importance is incomparably greater. The increased amount of urinary pigment excreted in fever (J. Vogel)—the fact that febrile urine contains an abnormal excess of potassium-salts (as much as sevenfold the normal proportion, when the fever is intense—Salkowski)—all this points to a great disintegration of the red corpuscles (Senator), since the coloring matter of the urine is derived from that of the blood, and the red disks (together with the muscles) are particularly rich in potassium. Febrile oligocythæmia, accordingly, is due to the simultaneous influence of inanition and consumption, and therefore not unfrequently attains a high degree of intensity. We know, besides, that the elimination of urea in fever is greatly increased; this important fact was first determined by Traube and Jochmann in a case of ague; it has since been fully corroborated, and extended to a great variety of febrile affections (intermittent, typhus, pneumonia, the acute exanthemata, pyæmia, acute rheumatism, etc.) by a number of independent observers (A. Vogel, Wachsmuth, J. Moos, Redtenbacher, Brattler, Ranke, Lemke, W. Mueller, Uhle, Sydney Ringer, Behse, Bartels, Huppert, et al.). And here it is important to observe that febrile patients, when kept on the same diet as healthy persons, not only produce and excrete a much greater quantity of urea than the latter (often two or three times as much), but also invariably excrete more nitrogen in the form of urea than they take in their food (Huppert), and that they cannot, therefore, be brought into a state of nitrogen equilibrium. In this respect they are like persons undergoing starvation, who, as is well known, though their supply of nitrogen is entirely cut off, continue nevertheless to decompose albumen and to excrete nitrogen while living at the expense of what Voit calls their "organ-albumen." The chief difference, as regards this matter, between fever and simple starvation is that the consumption of organ-albumen goes on far more actively in the former than in the latter; in other words, that the difference between the amount of nitrogen taken during fever, and the amount excreted, is much greater than the total amount of nitrogen excreted during absolute starvation (Huppert, Riesell, Senator). Accordingly the febrile process is invariably attended by a very rapid and excessive diminution in the amount of albumen in the system; this is a result, partly of inadequate nourishment—of inanition, partly and principally of the augmented consumption and decomposition of albuminates just alluded to.

The precise locality where the dissociation of albumen takes place in febrile maladies, and the mode in which it is consummated, are still doubtful. Huppert concludes from his researches on relapsing fever[1] that during the febrile state, stable "organ-albumen" is converted into unstable "store-albumen." The latter is then broken up; but the azotized products of its decomposition are not necessarily eliminated forthwith on the day of the fever. Since the increased elimination of nitrogen goes on for a time during the apyretic interval, and its maximum during the febrile period does not coincide with the acme of the fever, it is highly probable that the azotized product resulting from the decomposition of the albuminates is oxidized, not at once, but slowly and gradually, into urea. As regards the non-azotized products of decomposition, Huppert suspects that—in contradistinction to what happens in diabetes and acute poisoning by phosphorus—they undergo immediate oxidation in fever, thereby accounting, in some measure, for the increased production of heat.[1] Senator, on the contrary,[2] believes that the excess of heat is principally generated by the oxidation of the azotized products resulting from the decomposition of albumen; while the fatty matters simultaneously liberated remain to some extent unoxidized and contribute to the fatty degeneration of the tissues. He is disposed to reject the notion that any increased consumption of the non-azotized constituents of the body takes place in fever; but to this Acker very justly rejoins that it would be very difficult to account in any other way for the rapid disappearance of the *panniculus adiposus* in many febrile disorders (acute rheumatism). Any further discussion of this moot-point would be superfluous, since it does not in any way affect the doctrine of increased decomposition of organ-albumen, which may be viewed as quite established.

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[1] Archiv der Heilkunde. X. (1869) p. 506.

The next question is where the increased decomposition of organ-albumen takes place—or, to speak more accurately, which of the tissues furnishes the major part of the excess of albumen consumed? As regards this point, it may be as well to state that the blood itself, as a tissue, contains organ-albumen; nay, that the greater part of the albumen in the blood is organ-albumen (Voit), contrasted with which are the albuminates derived from the ingesta, forming the more unstable store-albumen. Accordingly, the increased consumption of organ-albumen in fever may affect either the organ-albumen of the blood, or that of the remaining tissues, or both at once. For, though it is exceedingly improbable that albumen is decomposed, under ordinary circumstances, while it is still in the circulating fluid (Hoppe-Seyler[3]), yet it is possible that in fever, particularly when caused by a zymotic poison, some part of the albumen of the blood may be decomposed immediately, without having previously formed part of the tissues; conversely, too, organ-albumen from the tissues may find its way back into the blood and be split up by the pyrogenic ferment circulating in the vessels. Lastly, it may be that in fever, as in health, the decomposition of albumen may take place chiefly in the tissues. All these points require to be further investigated, and must for the present be left uncertain. It is probable, however, on theoretical grounds, that the decomposition of albumen takes place—at any rate in the infective fevers—in the blood itself, the latter forfeiting a part of its own albuminates; further, that the organ albumen of the tissues is likewise decomposed *in situ*, the residual products of its decomposition—the non-azotized compounds—often remaining unoxidized in the tissues as fatty matter (Senator). Some such succession of phenomena would explain the acute origin of the anæmia, the rate at which marasmus is developed during the febrile state, and finally the frequent occurrence of fatty degeneration in various tissues.

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[1] Ibidem, p. 334.

[2] Untersuchungen über den fieberhaften Process und dessen Behandlung. Berlin, 1873. p. 135.

[3] Pflüger's Archiv. VII. (1873) p. 399.

But it is not only the urea that is increased during fever; the carbonic acid is increased likewise (Liebermeister, Leyden, Senator). Increased elimination of this gas is not sufficient of itself to prove increased production; but Liebermeister has shown, by investigations on febrile patients, that the increased elimination of carbonic acid begins before the actual onset of the febrile paroxysm; proving thereby that the phenomenon is not due to retention of the gas, followed by explosive exhalation. The same author has shown, moreover, that during the febrile paroxysm itself the increase in the amount of carbonic acid excreted does not proceed *pari passu* with the rise of temperature, but with the rate of heat-production; it follows, of necessity, that both phenomena, viz., increased elimination of carbonic acid and increased production of heat, must be due to the same cause, *i. e.*, increased oxidation of the substance of the body. We are unable at present to decide whether the excess of carbonic acid is chiefly furnished by the subcutaneous fat, or by the non-azotized products of the decomposition of albuminates; or, finally, by the azotized products of their decomposition likewise, while undergoing further degradation into urea. Indeed, it seems probable on clinical grounds that all of the above enumerated constituents take part together in the increased formation of the terminal product in question.

As evidence of the important fact that a marked increase in the production of carbonic acid takes place during a febrile paroxysm, I append the following determinations made by Liebermeister on one and the same patient (a man of forty-one, with a quotidian intermittent), before and during the paroxysm.[1]

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[1] Deutsches Archiv für klin. Medizin. VIII. p. 175.

Observation I.

	Axillary temperature at the close of each interval (Centigrade).	Increment of temperature during each period.	Carbonic acid excreted (in grammes).
In the 1st half-hour............	36.9°	0.1°	13.85
" 2d "	37.55°	0.65°	20.12
" 3d "	39.45°	1.9°	34.20
" 4th "	39.85°	0.4°	19.31
" 5th "	39.85°	0.0°	17.68
" 6th "	39.85°	0.0°	16.75

Observation II.

In the 1st half-hour............	37.0°	0.05°	13.00
" 2d "	37.1°	0.1°	13.77
" 3d "	37.75°	0.65°	20.59
" 4th "	39.4°	1.65°	31.07
" 5th "	39.5°	0.5°	18.09
" 6th "	40.2°	0.3°	19.42

In either table the amount of CO_2 excreted is seen to rise with the increment of temperature, and to attain its maximum at the beginning of the algid stage.

Lastly, an increased elimination of water takes place in fever (Leyden, Senator). During the febrile process, accordingly, a number of morbid changes go on side by side, and are more than sufficient, in the aggregate, to account for the deleterious effects of fever on the blood and other tissues. The changes in the blood are: oligocythæmia, hypalbuminosis, loss of volume, collectively amounting to anæmia in the usual clinical sense of the word. The changes in the tissues are those characteristic of marasmus—simple atrophy, more or less complete necrobiosis of the tissue corpuscles and their derivatives. Lastly, the peculiar relations subsisting between the various anomalies of molecular metamorphosis exhibited in fever—relations which I have just been trying to elucidate—explain the very exceptional significance of the febrile process in the production of anæmia and general marasmus.

Pathology.

General Outline of the Disease.

Anæmia may be acute, subacute, or chronic, according to its mode of onset and its course. The type assumed by the disease in any individual case will depend (apart from idiosyncrasy) on the intensity and character of its exciting causes.

The most acute variety of anæmia is that induced by sudden and profuse hemorrhage. When a relatively large portion of the total blood escapes rapidly from the vessels, the most extreme anæmia may be produced in a very few minutes. Should the bleeding be less severe, the symptoms of oligæmia are proportionately slower in making their appearance; but no one would hesitate to include under the "acute" category those cases in which manifest signs of anæmia declare themselves within a few hours, or even days (one to three), in consequence of protracted bleeding. The special character of any given case is accordingly determined by two main factors: the severity and the duration of the hemorrhage, for on them the course of the disease and the intensity of its symptoms chiefly depend.

The following are the principal causes of great loss of blood, and therefore of acute anæmia: (1.) Wounds, whether accidental or inflicted by the surgeon, that involve the larger vessels (especially arteries) or lay bare extensive surfaces; this includes secondary hemorrhage from the premature detachment of ligatures, imperfect coagulation of the blood in the vessels, etc. (2.) Accidents connected with pregnancy, delivery, and the puerperal state (*e. g.*, rupture of the Fallopian tube in tubal gestation, partial separation of the after-birth in placenta prævia, rupture of the uterus during delivery, adherent placenta, atony of the womb, etc.). (3.) Rupture or perforation of blood-vessels, occurring as grave but accidental complications of certain visceral diseases (*e. g.*, spontaneous rupture of the heart when in a state of fatty degeneration, bursting of internal aneurisms, ulcerative perforation of branches of the pulmonary artery in phthisis, profuse hæmatemesis in gastric ulcer and cancer, intestinal hemorrhage in enteric fever, etc.), or as a result of the so-called "hemorrhagic diathesis" (see chapter on Scurvy, Purpura, and Hæmophilia). Accordingly, acute anæmia may be developed, in a symptomatic form, in the course of a great variety of diseases, and may come under the observation alike of the physician, the surgeon, and the accoucheur.

The following are, broadly speaking, the symptoms of acute anæmia:

The skin and visible mucous membranes rapidly undergo a striking loss of color. The latter lose their natural rosy hue, while the skin of persons whose *rete Malpighii* contains but little pigment quickly assumes a waxy (yellowish white) paleness. Dark-complexioned people and members of the dark-skinned races, on the other hand, appear rather darker than usual; the former, *e. g.*, exchange the lively carnation of health for an earthy or dusky (grayish yellow) tint. Together with the loss of color, the skin and superficial soft parts lose their normal "turgor." Hollow cheeks and sunken eyes, a projecting and very pointed nose, are common phenomena, and give the patient a strange and spectre-like expression. The skin, especially over the more prominent parts of the face (nose, ears) and extremities, feels cold to the hand; the entire body is often as cold as a corpse, and a thermometer introduced into the axilla or rectum registers an unusually low degree of temperature (temperature of collapse). The cold skin may be dry; more commonly, however, it is bathed in a clammy perspiration—the so-called "cold sweat"—which forms a striking contrast to the anæmia of peripheral parts, their low temperature, and the state of the pulse. The latter quickly becomes very small in the superficial arteries. For a time it may be rather hard, but it soon grows very compressible, and may even cease to be felt. Its rate is usually somewhat accelerated, the number of beats undergoing great and sudden increase when the patient makes any exertion or assumes the erect posture. Should he faint, loss of consciousness is almost always preceded by a sudden alteration in the pulse, which becomes slow, intermittent, and, during the actual syncope, imperceptible. The heart's impulse resembles the pulse, it becomes feeble, cannot be found without difficulty, and only exhibits a transient intensification during emotional excitement or bodily exertion. Its rhythm undergoes the peculiar fluctuations alluded to above. On auscultation (when the patient is at rest), the sounds of the heart are faint and muffled; the first sound, more especially, may be almost or altogether inaudible; the second sound can usually be heard so long as the patient is alive. Should the heart be temporarily excited, the first sound is generally replaced by a blowing murmur heard all over the præcordia (anæmic or accidental murmur). The "bruit de diable" may be detected in the veins of the neck.

Other symptoms of an important kind speedily show themselves in connection with the voluntary muscles and the nervous system.

When a healthy man is suddenly and unexpectedly deprived of a quantity of blood while standing or walking, he usually loses the power of maintaining the erect posture in a few seconds or minutes, all his muscles become relaxed, he staggers and sinks to the ground. This is seen when a man is wounded on the battle-field or in a brawl, and suddenly loses a quantity of blood. Should the bleeding be less profuse, muscular power—at any rate, in a vigorous subject—may be retained for a longer time. The bleeding man drags himself along for some distance, until, overpowered by a sense of weakness, his muscles refuse their office and he succumbs altogether. The phenomena are somewhat different in the case of a man confined to bed by previous illness, and already suffering from symptoms of anæmia. The change is less striking and abrupt; but the rapid failure of muscular power is nevertheless betrayed by increasing tremulousness on movement, by his slipping down in his bed, by his weak, muffled voice, etc.

When much blood has been lost, the weakness usually culminates in actual syncope, during which consciousness is wholly abolished, the patient resembles a corpse, the heart's action is reduced to a minimum, respiratory movements cease, and real death not unfrequently ensues. The attacks of syncope sometimes occur with lightning-like suddenness, almost without warning. More commonly, however, they are preceded by the usual prodromata, consisting—apart from the circulatory phenomena already described—in seeing flashes of light before the eyes, and tinnitus aurium, followed by dimness of vision and loss of hearing. Should the patient be restored to consciousness, he often faints away again immediately, especially if he attempts to rise, or is raised by those about him. Mental excitement is a less frequent result of loss of blood; occasionally, however, there may be furious delirium. Symptoms more commonly met with are troublesome hiccough, nausea, and even actual vomiting (the latter chiefly when the patient assumes the erect posture), also a painful sense of præcordial anxiety and dyspnœa, the latter frequently attended by an objective quickening of the respiratory movements. In many exceptionally sudden cases of hemorrhagic anæmia, severe general convulsions of an epileptiform character set in just before death, after the patient has become unconscious; but it is more common, upon the whole, for death to occur during a state of unconsciousness and universal prostration, without convulsions, or, at any rate, with only a slight twitching of the muscles.

The patient may die either at once, or after some hours or days, with the above symptoms, or he may be lucky enough to survive when the bleeding has ceased spontaneously or has been stopped by art. In the latter event, the period of threatening weakness and collapse is followed by one of reaction, whose signs are at first barely perceptible, but steadily grow more and more distinct.

The earliest sign of rallying is usually given by the pulse, which gradually becomes somewhat fuller; the skin grows warmer, and the sweating abates. The patient's shrunken lineaments assume a more natural expression as the soft parts become turgid; but the skin and mucous membranes continue very pale and do not regain their natural hue for weeks or months. The patient remains feeble and languid for a long time. He is not out of danger, even though there may be no risk of fresh hemorrhage. Fatal syncope may occur quite unexpectedly at any moment. Fortunately, however, such fainting-fits are not invariably fatal. They are brought on by exertion, by hasty efforts to get up, by straining at stool. The premonitory symptoms often show themselves without being followed by loss of consciousness. I refer to the sensory disturbances described above, to the sudden pallor, to the breaking out of a cold sweat, etc. Strength returns very slowly and gradually. Even after its partial restoration, any slight effort is followed by fatigue. Muscular exertion during a few minutes causes a feeling of oppression at the chest, panting respiration, palpitation of the heart. The face, usually pale, grows flushed; the patient feels his forehead, his cheeks, perhaps his whole body, become hot; he often begins to perspire profusely, although at other times he is more inclined to shiver and to complain of cold feet.

Immediately after a great loss of blood, and during the first days of convalescence, the patient suffers from burning thirst and a fierce craving for liquids; but he has no appetite for food. This does not return till later, and then it frequently amounts to positive voracity—a paroxysmal bulimia. As a rule, however, the patient's powers are unequal to his desires; notwithstanding his imperious craving for food, a sense of repletion comes on very soon—often after a few mouthfuls—and may even amount to discomfort, oppression about the stomach, eructation, or even vomiting. Catarrh of the stomach is not uncommon, especially after any error of diet. It manifests itself by a furred tongue, complete anorexia, perhaps even fever. The intestines, too, are very susceptible, and the usual tendency to constipation is occasionally interrupted by unexpected attacks of diarrhœa, whenever the patient is at all careless about the quantity or quality of his food. The signs of so-called "atonic dyspepsia" are usually very slow to disappear. It takes a long time for the digestive apparatus to regain its pristine faculty of dealing with considerable quantities of any sort of nourishment.

The secretion of urine is at first extremely scanty, but it gradually increases in amount as time goes on. Curiously enough, analysis of the first urine passed after the occurrence of hemorrhage shows an increased formation of urea (J. Bauer). Subsequently, however, after the patient has begun to rally, the total amount of urea and other solids is lessened, and the urine is correspondingly pale and of low specific gravity. This, too, is transient, and subsides as the organism returns to its normal state.

The nervous system shows manifold signs of disturbance during the period of convalescence; these signs, however, are so protean as to elude any complete enumeration. Some of the changes produced involve the nervous system as a whole; others are more localized, and a few are anatomically circumscribed in the most precise way. Roughly speaking, the symptoms of "nervous irritation," or, more correctly, of "irritable weakness," predominate over those of simple paresis or actual palsy, and the combination of exalted irritability with proneness to be speedily exhausted is pretty uniformly displayed by the most various parts of the nervous apparatus. General hyperæsthesia is a common symptom. Its intensity depends, not merely on the degree of anæmia present, but also on the previous state of the sensory system, and is therefore most marked in women, children, and persons of nervous constitution. This is likewise true of the exalted reflex irritability, which occasionally amounts to actual spasmophilia. Localized forms of spasm, though sometimes met with, are not common. Pain, on the other hand, is very common, and presents itself in every conceivable form and situation—now vague and rheumatoid, now localized in the head, back, teeth, etc. When localized, it often assumes the characteristics of a true neuralgia; it is paroxysmal, lancinating, and follows the distribution of a particular nerve. The nerves of the internal viscera are also liable to be affected by neuralgia in anæmic persons. The forms of neuralgic pain are not distinctly localized. Their connection with the altered state of the blood is proved by their disappearing during the progress of convalescence. Among them nervous cardialgia takes a prominent place, both on account of its frequent occurrence in anæmic patients, and because it is usually confounded with gastric ulcer. Lastly, the abnormal irritability of the nervous system often shows itself in the patient's mental condition. Broken sleep or obstinate sleeplessness, a quarrelsome and self-willed temper in the waking state, all sorts of whims and fancies, are as common as they are annoying both to the patient and to those around him. Occasionally the psychical disturbance amounts to positive eccentricity, verging on actual madness, and sometimes transgressing the boundary line between the two.

I must add a few words about the nutrition and bulk of the patient's body. Should he survive the immediate effects of the loss of blood and fairly enter on convalescence, he becomes very liable to slight œdema, especially of the lower limbs, less often of the face and hands, which gradually disappears as he gets better. When this slight dropsy is present, it tends to mask the positive decrease in bulk which would otherwise be apparent, and which, after persisting for a while, ultimately yields to care and feeding. It must, however, be admitted that the marasmus associated with acute anæmia is always much less marked than that developed in connection with the subacute and chronic forms of the disease. Some wasting of the muscles, indeed, there is ; but the subcutaneous fat is scarcely affected, the contrast between the patient's excessive pallor and his relatively plump appearance being often most characteristic.

The above description of acute anæmia after profuse hemorrhage embraces many features (if we put aside the earliest symptoms and take those alone that occur during the stage of convalescence) which may be transferred to the subacute and chronic forms of the disease. The symptoms of the two latter are for the most part the same as those enumerated above ; what differences there may be depend partly on the different rate at which the symptoms, taken altogether, are developed, partly on the different degree to which they attain individually—these conditions, in their turn, being principally regulated by the nature, duration, and intensity of the causes in operation. The ensuing paragraphs will be mainly devoted to a consideration, however fragmentary, of these differences, for, as I have already said, a detailed description would take us much too far.

Subacute anæmia (requiring from one to three weeks for its development) may be caused by small but repeated hemorrhages, or by albuminous discharges when very abundant. It may likewise be brought on—and more rapidly than by discharges—by the graver forms of pyrexia, of whatever kind. Besides these symptomatic varieties of subacute anæmia, there is also a class of idiopathic cases in which the disease results from extreme lack of food, or lack of food in conjunction with severe fatigue, exposure to cold, and other debilitating influences.

Chronic anæmia includes all those states of oligæmia and general marasmus which come on more slowly and gradually than those described above, or which, after setting in more or less abruptly, linger on without appreciable change for weeks, months, or years. This class includes most cases of idiopathic anæmia; also those symptomatic forms of the disease which result from moderate discharges, malignant growths, parasites, non-febrile dyspepsia, disorders of the circulatory organs and of the spleen, etc., and lastly, from protracted though not very severe pyrexia. That the chronic class includes a majority of all cases of anæmia is obvious from the number and variety of causes just mentioned.

The symptoms of subacute and chronic anæmia consist, in the first place, like those of the acute variety, in certain characteristic changes of the outward habit. These changes take a longer time to make their appearance; when present, they tend to last for a longer period. The skin and visible mucous membranes lose their color, but they rarely become as pale as they usually do after great loss of blood.

Those forms of chronic anæmia which result from profuse discharges (especially severe albuminuria), malignant growths, and diseases of the spleen and lymphatic glands, stand nearest to acute anæmia in this particular. Even in these cases, however, extreme decoloration of visible parts is not usual, save in association with considerable dropsy, or towards the end of life.

Diminished "turgor" of soft parts may likewise be observed. But dropsy often sets in sooner or later, and the patient comes to exhibit a puffy aspect. The dropsy is sometimes considerable, and extends from the skin and subcutaneous tissues to the serous cavities, and ultimately to many of the internal organs likewise (especially the lungs and the brain).

All the varieties of subacute and chronic anæmia do not lead with equal frequency to dropsy; neither does the dropsy attain its maximum degree of development with equal facility in all. In this respect, anæmia due to renal disease with great albuminuria and lessened secretion of urine (especially croupous and parenchymatous nephritis) stands foremost; indeed, this statement may be generalized to include all states o1 marked hypalbuminosis resulting from a profuse drain of albumen from the blood, without proportionate loss of water. A minor degree of dropsy is very common in the anæmia caused by cancer, but its appearance is usually deferred till death is at hand. Slighter degrees of dropsy are also met with, though more rarely, in a great many other forms of anæmia, but they are not of much clinical importance. On the other hand, dropsy is most unusual at the height of acute febrile maladies; after the fever has gone down, however, the oligæmia which persists during convalescence is not uncommonly attended by slight œdema, especially about the ankles. (Concerning the mode in which so-called "marasmic dropsy" originates in anæmic patients, see the section on Symptomatology.)

One of the most important and constant symptoms of subacute and chronic anæmia is the marasmus by which the patient gradually becomes affected. The patient's nutrition almost always suffers in proportion to the duration of the anæmia; the pallid or earthy hue of his skin becomes associated with a more or less severe degree of emaciation. Wherever the skin is not œdematous, it becomes thin and wrinkled, and falls readily into folds; the subcutaneous fat disappears; the muscles waste and grow flabby; in a word, the previous roundness and fullness of outline are effaced, while the skeleton grows more and more distinct. I may add that the different forms of oligæmia, according to their respective causes, exhibit marked differences both as regards the degree of liability to marasmus and the rate at which it is developed.

Of all the causes of anæmia, fever, as I have already pointed out, leads most rapidly to a considerable degree of marasmus. Protracted fever, such, *e. g.*, as usually attends pulmonary phthisis, is therefore, in the fullest sense of the term, a "consumptive fever" (Zehrfieber). A similar degree of marasmus may also be met with in cases of anæmia caused by malignant growths, or by obstacles to the introduction of food, or by obstinate diarrhœa; but the emaciation in these and analogous cases is incomparably slower in the rate of its development. The state of the patient's nutrition is relatively least affected in those forms of anæmia which are due to primary disease of the cytogenic organs, so long as this is unattended by fever.

The hair and the nails very frequently take part in the marasmic condition of the skin. They lose their normal lustre; the hair of the scalp usually falls off—thinning, or even partial baldness, transient or permanent, being produced. The nails, on the other hand, are seldom shed; but the growing part of the nail is often thinned, so that its surface comes to present grooves and furrows; sometimes a claw-like curvature of the entire nail ensues. As regards the secretory activity of the skin, it may be laid down as a rule that the sebaceous secretion is usually checked in anæmic marasmus, while the function of the sudoriparous follicles is not affected in any constant way; indeed, the latter seems to be but little influenced by the presence of anæmia. The insufficiency of the sebaceous secretion is manifested by a brittle state of the superficial layers of the cuticle, passing readily into branny desquamation (*Pityriasis tabescentium*). Lastly, the temperature of the skin is usually low (except in most cases of febrile anæmia); the patient is susceptible to cold, prone to shiver, and not unfrequently exhibits subnormal temperatures.

When the anæmia is progressive, this tendency to a low temperature grows more and more apparent; it may even show itself in fever, by a gradual reduction in the evening exacerbations. (Cf. the remarks on this point in the section on *Symptomatology*.)

As regards the functions of most of the internal organs, I need say no more; for the symptoms that start into prominence during recovery from acute anæmia are, for the most part, also present in the subacute and chronic forms of the disease. Only it must be borne in mind that phenomena which present themselves in acute anæmia as transient pathological residues of an antecedent catastrophe, are here of a more stationary or even progressive character, without being on this account essentially different in kind.

Thus, for example, the heart and vascular system present all the symptoms described above, the most characteristic of which, as the reader may recollect, were the feebleness of the heart's impulse and of the pulse in the arteries, the tendency to syncope, the excitability of the heart, the systolic murmurs, and the *bruit de diable* in the jugular veins. Peculiar to many cases of anæmic marasmus are: a tendency to spontaneous coagulation of the blood ("marasmic thrombosis"); a liability to hypostatic congestion, or gravitation of the blood to dependent parts, owing to which serious pulmonary complications may arise (hypostatic œdema and pneumonic infiltration); lastly, the occasional development of a "hemorrhagic diathesis," manifesting itself by bleeding from the mucous membranes (especially epistaxis) or petechiæ in the skin. Should the bleeding be profuse, symptoms of acute anæmia may be superadded to those of the subacute or chronic form, and the patient's life may be endangered.

As regards the respiratory and the digestive organs, I can add nothing of importance to what I have already stated. Digestive troubles, when they do not happen to be among the causes of the existing anæmia, often arise as a result of the various subacute and chronic forms of the disease. The appetite is seldom good; the patient is commonly tormented by the "atonic dyspepsia" alluded to above, even though true gastric catarrh may not be present, for the dyspepsia puts obstacles in the way of his being sufficiently nourished.

Concerning the voluntary muscles and the nervous system, I may refer the reader to my previous statements. Inability to bear fatigue, and actual weakness, together with that long train of symptoms indicating nervous irritability with inadequacy of nervous function (collectively termed "irritable weakness"), are among the most common features of every variety of anæmia; they differ in degree according to the severity of the disease and the constitutional idiosyncrasy of the patient.

The urine is not generally much altered in quantity, but it is deficient in soluble constituents and coloring matter. Febrile anæmia is, of course, an important exception to this statement. The main characteristic of febrile urine—its concentration, due to an increased proportion of urea and coloring matter—is always present. Another exception is the anæmia due to disease of the kidneys; the presence of albumen, formed elements, etc., introducing essential modifications into the composition of the urine, while its quantity varies widely in the different forms of renal mischief. Such deviations from the normal standard I need only mention; they need not be described, as their connection with anæmia is very indirect.

The function of the generative organs is often disordered in anæmic persons; but these disorders are not always the same, even in the same sex. In the male, abnormal erethism, manifested by involuntary emissions and premature ejaculation during coitus, is not uncommon; it forms part of the "irritable weakness" of the nervous system. Sometimes, however, the sexual appetite is lessened, or even quite extinguished. In the female, the menstrual flow is often less abundant; sometimes it is arrested; but profuse menstruation or even menorrhagia are just as common. The latter, of course, will tend to intensify the existing anæmia. Finally, many anæmic women and girls suffer from leucorrhœa, which must be attributed to the altered state of the blood; for it often makes its appearance after the anæmia has lasted for some time, and yields to tonic treatment without any local remedies. On the other hand, a profuse leucorrhœal discharge must needs react unfavorably on the very anæmia of which it is a result.

The general course of subacute and chronic anæmia varies widely in individual cases and in different forms of the disease; it is chiefly determined by the nature of the efficient causes. Some forms are progressive (*e. g.*, the anæmia associated with malignant growths, with hectic fever, with incurable organic disease), and terminate sooner or later in death from exhaustion. Others improve after an interval; and, if their causes have been removed in time, issue in complete recovery. In others, again, the improvement is but partial; either because complications or sequelæ become developed, or — and this is more common — because a certain degree of anæmia and debility persist obstinately, in spite of all remedies and notwithstanding the removal of the original causes of the malady. In the sections on *Duration*, *Issues*, and *Prognosis*, I shall endeavor to elucidate the causes of this peculiar behavior of some varieties of anæmia.

Anatomical Alterations.

I shall begin with a brief account of the post-mortem appearances in acute and chronic anæmia, limiting myself to those that result from the blood-change and not from any collateral disease (as in the symptomatic forms of anæmia).

The body of a patient who has succumbed to acute oligæmia after hemorrhage shows no signs of emaciation unless the hemorrhage has been preceded by some exhausting malady. When a healthy man in the full bloom of life has bled to death by accident, *e. g.*, from a wound, the well-nourished condition of his body forms a striking contrast to its extreme bloodlessness. When death has been ushered in by general convulsions, rigor mortis comes on early, and is usually well-marked; on the other hand, when death occurs during a state of prostration by the gradual extinction of the functions most important to life, rigor mortis is generally slight, and is late in making its appearance.

The peculiar decoloration of the skin, so obvious during life, is still more apparent after death. Of course it varies, as I have already pointed out, with the original complexion, *i. e.*, with the amount of pigment in the skin. Post-mortem staining is either absent or inconspicuous; cadaveric hypostasis, usually visible in dependent parts, especially about the buttocks, is wanting. The internal parts are likewise bloodless; here and there we find a region into which what blood there is seems to have gravitated (especially the postero-inferior parts of the lungs, the parts in the hinder fossæ of the skull, the spinal cord). The extreme bloodlessness brings out the proper tint of every organ, as it does that of the skin; the kidneys are pale yellowish red on section, the liver of a light brown or buff color, the spleen of a pale brick red. On the other hand, many differences of hue depending on vascularity, which are generally most striking, are obliterated; *e. g.*, the gray and white matter of the brain, the cortical and medullary portions of the kidneys, are less sharply marked off from each other in the body of an anæmic person than they generally are. When any organ is cut into, the quantity of blood that oozes from it is exceedingly small; the tissues generally are drier, firmer, and rather more compact than usual. The diminution in volume is more marked in some organs than in others, *e. g.*, in the spleen, whose capsule is wrinkled, and therefore looks as if it were thickened. There is very little blood in the heart and great vessels; the latter are frequently empty, while the cavities of the former contain only a few pale coagula. The heart is often very firmly contracted, smaller than usual, and with its walls proportionately thicker; in other cases, again, especially when the patient has been long in dying, the heart is found relaxed and of its ordinary size.

The microscope detects no structural alterations whatever in the organs of a man who has bled to death. Should the fatal issue have been delayed (*e. g.*, for a few days), or caused by a fainting-fit during the stage of convalescence, signs of incipient or even advanced fatty degeneration may be found in the muscular substance of the heart, the inner coat of the great vessels, the gastric glands, the hepatic cells, and renal epithelia. When severe oligæmia has lasted any time, such appearances are very common (*vide infra*). Under similar circumstances, there may be some dropsy ; slight œdema may be apparent about the legs, together with some ascites or hydropericardium. Any considerable amount of dropsy, on the other hand, is as uncommon as well-marked emaciation or marasmus.

Subacute and chronic anæmia due to other causes exhibit a greater variety of post-mortem appearances. The following general indications must suffice :

The body, as a rule, is slightly rigid, marked by a few rosy stains. Cadaveric hypostasis is either absent or slight. The surface is of a pallid or earthy hue. There is nearly always some emaciation, manifested (in the absence of dropsy) by the skin being thrown into folds, the subcutaneous fat being thin, the muscles wasted. The marasmus is occasionally extreme (especially in cancerous or phthisical patients), the complete absence of subcutaneous fat and the wasted condition of the muscles making the corpse resemble a skeleton loosely wrapped in skin. When the marasmus is less severe, it may be altogether masked by œdema. Dropsy is most common in those forms of anæmia which are caused by a drain of albumen from the blood (through the kidneys, bowels, etc.). It shows itself in the well-known form of tense œdema of the superficial soft parts, and thus prevents any accurate estimate of the degree of emaciation present ; but, if we cut into the dropsical tissues, they often shrink into a surprisingly small bulk as the serum pours from the incision.

While considerable anasarca is chiefly limited to certain special forms of subacute and chronic anæmia, minor degrees of puffy œdema, particularly of the lower limbs, are often noticed in connection with every variety of oligæmia. Internal dropsy obeys the same law, for, while a moderate degree of ascites, hydrothorax, hydropericardium, etc., is a common post-mortem appearance in anæmia of the most diverse origin, copious effusion into those cavities is almost entirely confined to those more definite forms of oligæmia which are distinguished by an exceptional development of the so-called "hydræmic crasis." I may add that both observation during life and post-mortem inspection furnish numerous exceptions to the ordinary rule in both directions. Dropsy is occasionally absent when it might fairly be expected to occur; sometimes it is very severe without its usual causes having been in operation.

Besides the possible discovery of dropsical accumulations, post-mortem inspection may disclose one or more of the following appearances:

The quantity of fat in those deeper parts where it usually accumulates—*e. g.*, the visceral layer of the pericardium, the great omentum, the perirenal tissue—may be reduced, as it is in the *panniculus*. In extreme marasmus the fat may have altogether disappeared, leaving nothing but empty areolar tissue behind. The latter, under such circumstances, is glassy and translucent, and of jelly-like consistency. Moreover, the internal organs may be more or less anæmic, presenting those variations in color and bulk which have already been referred to. The bloodlessness is associated with actual wasting, with a positive diminution in the size and number of the textural elements, ascertainable with certainty by careful microscopical examination. The degree of atrophy, measured by loss of weight, varies considerably in different organs, and is, upon the whole, far less than the wasting of the adipose tissue; on the other hand, it is greater than that of the voluntary muscles. The spleen appears to lose most, the brain least weight in marasmic conditions of the system, always excepting those symptomatic forms of anæmia in which the results may be complicated by the primary disease. (For details, consult the section on *Special Symptomatology*, under the head "Marasmus").

The heart and great vessels contain less blood than usual, but more, upon the whole, than they do in acute anæmia after hemorrhage. The coagula are often pale in color, lax, and poor in precipitated fibrin; blood, which is still fluid, may be present with them. The heart is usually small and relaxed; its tissues, including the *columnæ carneæ* and *musculi papillares*, wasted and pale; the right ventricle, however, is not seldom found moderately dilated and with its walls considerably thinned, making the organ, as a whole, appear broader than usual.

I have still to allude to a peculiarly interesting group of structural alterations, indicating degeneration of tissue elements. Such alterations are often met with after death in cases of subacute and chronic anæmia, and may be most satisfactorily studied in the muscular substance of the heart and in the arterial system.

Under the name of "anæmic fatty heart," Ponfick describes a diffuse form of fatty degeneration of the cardiac muscle, unattended by hypertrophy or valvular mischief, which occurs in connection with every variety of severe and protracted anæmia. It differs from the senile form of fatty heart in not being associated with chronic *endoarteritis deformans*. It presents itself as an independent disease of the heart. Amid the muscular tissue which has undergone diffuse alteration, but whose fibrillæ do not generally exhibit any very advanced degree of fatty change, we come across a variable number of patches in which the degeneration is extreme. These patches are chiefly situated in the *musculi papillares*, and may be recognized, even with the naked eye, as yellowish, opaque spots and striæ. Side by side with these degenerative changes in the muscular tissue of the heart we usually find alterations of an analogous kind in the intima of the aorta and large arteries generally; sometimes, though less frequently, in their middle coat as well; lastly, we may detect partial fatty degeneration of the capillaries (more especially in the brain).

The changes in the aorta will be described more fully when we come to treat of the post-mortem appearances in chlorosis. In this peculiar form of anæmia the anatomical condition of the arterial system possesses an exceptional degree of clinical and etiological significance, and embraces far more than the degenerative processes alluded to above. I may just mention here that the opaque, yellowish spots and striæ, by which the unarmed eye is able to distinguish those parts of the arterial intima which have undergone fatty change, are found, on closer inspection, to consist of innumerable yellowish dots, every one of which corresponds to a connective-tissue corpuscle in a state of fatty degeneration (Virchow).

But traces of fatty change or signs of advanced degeneration are also met with elsewhere, *e. g.*, in the renal epithelia, the hepatic cells, the epithelia lining the tubular gastric glands, etc. (Ponfick). That these tokens of slight or severe parenchymatous degeneration are really due to the anæmia may be inferred from the fact that they coexist with the most diverse forms of this disease. Moreover, it has been shown by experiment on animals that the alterations in question are invariably produced, sooner or later (Perl, Manassein), in consequence of severe anæmia of artificial origin (copious and repeated bleeding, starvation). Hence, there can hardly be a doubt as to the causal relation between the altered state of the blood and the tissue-changes.

Perl bled dogs at intervals of from five to seven days, taking at every operation a quantity of blood equivalent to three per cent. of the body weight; at the end of two months post-mortem examination furnished distinct evidence of fatty degeneration of the heart, besides well-marked marasmus. It should be added, however, that the former change was only met with in such animals as had been rather freely bled at considerable intervals. Vigorous and well-fed dogs, from which smaller quantities of blood had been taken (1 to 1.5 per cent. of the body-weight) remained quite lively, and presented no morbid changes after death. In the dog, as in the human subject, the fatty degeneration was usually most marked in the *musculi papillares*, but it was less advanced in the former than in the latter; for whereas in man the fatty change manifests itself in the form of opaque yellowish spots and striæ, in the dog it is diffuse and more moderate in degree. The *musculi papillares* were always found more severely affected on the left than on the right side of the heart; the same difference was noticed between the muscular walls of the two ventricles; lastly, the walls of the right auricle were least altered.

Manassein had previously noticed that in rabbits deprived of food, fatty degeneration speedily attacks the renal epithelia (tube-casts making their appearance in the urine); similar changes take place in the hepatic cells, the tissues of the voluntary muscles and of the heart—even in the corpuscular elements of cartilage. These histological data may be transferred from the lower animals to man, the fatty degeneration of the tissues so frequently met with in anæmic patients being likewise attributed to the impoverishment of the blood and the state of inanition to which the organs are reduced. (Further details on this subject will be given in the ensuing section.)

Special Symptomatology.

(Analysis of the Individual Symptoms and Post-mortem Appearances.)

The immense variety of pathological phenomena presented by anæmia may be most easily and naturally reduced to order by a classification under three heads: *First*, we must consider the altered properties of the blood itself, tracing them to their source in those primordial disturbances whose conjunction forms the essence of anæmia (Cf. *Introduction*). *Secondly*, as a result of the blood-change we find a series of constitutional symptoms, among which are the comparative bloodlessness of the different organs, the dropsy, the failure of tissue nutrition, the reduced level of temperature, etc. *Thirdly*, in contrast to these constitutional phenomena, we have a set of local symptoms whose intimate connection with particular organs and systems renders it necessary to group them anatomically. I shall follow this order in the ensuing pages, and try to furnish an analysis of the more important phenomena of the disease, so far as the existing state of our knowledge and the limited space at my disposal will permit.

I. *Alterations in the Blood.*

1. *Color.*—The blood of an anæmic person, whether examined during life or after death, is of a brighter tint than usual. The paler hue of the blood must, of course, be attributed to the diminished amount of coloring matter it contains, and—since the hæmoglobin is contained in the red corpuscles—to an abnormal condition of these elements. This, in its turn, may consist either in a numerical diminution of the red disks (oligocythæmia) or in their containing an abnormally low proportion of hæmoglobin (oligochromæmia). As a fact, the two deviations from the healthy standard appear to co-operate in producing the paleness of anæmic blood. As regards the anæmia due to hemorrhage, indeed, Vierordt has found, not only that the proportion of red disks (ascertained by direct enumeration) under-

goes progressive diminution as the anæmia is more and more severe, but also that the individual corpuscles become visibly paler in hue, whence they may be inferred to contain less hæmoglobin. Of course, we cannot be sure that the red disks undergo similar changes in other forms of anæmia as well; we do not know in which of them we may assume a similar combination of oligocythæmia with oligochromæmia to exist. Hence, we must not exceed the general statement that the brighter color of the blood in most cases of so-called anæmia is due to a diminished percentage of hæmoglobin in that fluid, leaving it for future inquiries to decide on the exact mode in which this diminution comes about. Inasmuch, however, as the physiological function of the red corpuscles is primarily dependent on the hæmoglobin they contain, it follows that any reduction in the percentage amount of coloring matter in the blood (ascertained roughly by mere inspection, more precisely by chemical analysis according to the method of Becquerel and Rodier, or by means of Vierordt and Welcker's color scale) must be clinically equivalent to true oligocythæmia. By thus extending our conception of oligocythæmia so as to make it include oligochromæmia, we may safely infer its presence (as, indeed, we do daily) from the altered color of the blood.

Neither here nor elsewhere can I describe the various methods employed in the chemical analysis of the blood. The reader who desires to become acquainted with this important branch of physiological chemistry must consult the writings of the authors I have named above, and the text-books devoted to the subject.

The pale tint of the blood in any individual case must obviously be proportionate to the degree of importance assumed by oligocythæmia among the primary changes taking place in the nutrient fluid. Those causes of anæmia which operate injuriously on the red corpuscles will therefore stand foremost in robbing the blood of its color. Such causes are: loss of blood by hemorrhage, toxic and infective processes, disease of the cytogenic organs, fever; but, as I have already pointed out (in the section on *Etiology*), *all* the causes of anæmia, directly or indirectly (as by giving rise to hypalbuminosis) tend, sooner or later, to induce oligocythæmia. Hence, the color of the blood in anæmic patients will nearly always be paler than that of the blood in health. The only possible exception to this rule may occur in cases where the oligocythæmia is associated with great loss of water. The increased concentration of the blood may enable it to retain its depth of color, notwithstanding the loss of a large proportion of its hæmoglobin. Conversely, the retention of water (as in many forms of renal disease) may cause the blood to appear pale without any reduction in the total number of the red corpuscles. Lastly, the paleness of the blood in leukhæmia is due partly to an *oligocythæmia rubra*, partly to an absolute increase in the number of leucocytes. Now, if we put aside those peculiar cases in which the oligocythæmia is in a measure *relative*, we may lay it down as a rule that paleness of the blood is characteristic of anæmia; that it is nearly always due to an *absolute* oligocythæmia, and that it constitutes an approximative measure of the degree which the latter change has reached.

2. *Quantity.*—The total volume of the blood is usually reduced in anæmia. In many forms of the disease, indeed (*e. g.*, acute anæmia after hemorrhage, anæmia of the last stage in the cancerous cachexia, anæmia due to protracted fever), the reduction—as proved on post-mortem examination—is extreme. In other forms, again, it is relatively insignificant when compared with other changes, *e. g.*, with the loss of color or the degree of dilution (anæmia caused by disease of the spleen and lymphatic glands, that due to exhausting discharges, etc.). Any exact determination of the total volume of the blood during life is obviously impracticable, and all but impracticable even after death. Our estimate in any given case must always be highly approximative. If we proceed to inquire how the volume of blood comes to be reduced in anæmic conditions of the system, we shall find the sequence of events very clear in one form of the malady, viz., acute anæmia after profuse bleeding. I need hardly bring evidence to prove that a rapid and abundant hemorrhage must needs diminish the quantity of blood in the body (though not by any means in direct proportion to the amount of blood lost, p. 327). But even when the anæmia is due to repeated losses of smaller quantities of blood—still more when it is due to other causes than hemorrhage—the total volume of

the blood is found to be reduced, and we have to explain how this is brought to pass—what are the conditions that lead to a diminution in amount of the most voluminous constituent of the nutrient fluid, viz., water. Even admitting that many of the noxæ that induce oligæmia in the clinical sense of the term, *e. g.*, exhausting discharges, withdraw a quantity of water from the blood, there does not seem to be any reason why a corresponding amount of water should not be taken up from the tissues or the stomach to make good the deficit. Nay, there is plenty of direct evidence to show that such compensation is continually going on; so that when we find symptoms during life (especially the state of the pulse) and appearances after death pointing to a permanent reduction in the volume of the blood, we cannot but regard the facts as singular and enigmatical. None the less is it true that the prime cause of the phenomenon has already been mentioned (p. 311)—it is the hypalbuminosis of the blood. A certain portion of the water of the blood is fixed in and incorporated with the albuminates of the plasma in virtue of their colloid nature. It is thereby rendered in a certain sense permanent. The residual portion of the water is subject to great temporary variations in consequence of absorption from the stomach, etc. Hence, the average volume of the total blood is primarily regulated by the proportion of albuminates in the plasma, and must therefore be reduced by the presence of absolute hypalbuminosis. Now, as most of the causes of anæmia induce hypalbuminosis as their primary and direct result, they must necessarily (apart from counteracting influences) tend to diminish the total volume of the blood. Moreover, the saline ingredients of the plasma stand in some ill-understood relation to the osmotic phenomena going on in the organism, and exert an influence upon the elimination of water through the skin and kidneys, and thus upon the volume of the blood. Now it has been shown by C. Schmidt that the salts of the blood stand in a definite reciprocal relation to its albumen, one part of salts being taken up from the tissues for nine parts of albumen withdrawn from the blood. The connection between the volume and the centesimal composition of the blood thus assumes a more complex aspect, and cannot be explained by the degree of hypalbuminosis alone. Finally, the elimination of water through the kidneys, lungs, or skin may be interfered with—or facilitated—in many cases of anæmia, by local disease in those organs. Thus we see that no very simple answer can be given to the question concerning the way in which the total volume of the blood becomes diminished in the different forms of anæmia. So much we may safely assert, that any hinderance to the excretion of water, such, *e. g.*, as is offered by many diseases of the kidneys, tends to oppose any lessening of the volume of the blood; unless, of course, the simultaneous occurrence of dropsy neutralizes the accumulation of water in the vascular system. (*Vide infra.*)

3. *Other properties of the blood* (consistency, coagulability).—Besides being paler in color and reduced in volume, the blood of anæmic persons is usually thinner than normal blood, and coagulates more slowly and less firmly. These features are commonly noticed after death as well as in life. The smaller proportion of colored elements suspended in the plasma, the lessened quantity of albuminates, the increased amount of water—these are doubtless the causes of the thinness of the nutrient fluid. (Cf. the observations made above concerning the possibility of an increased percentage of water in the blood.) Again, the indisposition of the blood to coagulate, and the scanty clots formed, point to a simultaneous diminution of its fibrinoplastic properties and of the quantity of fibrinogen it contains. Since the fibrinogen is probably conveyed to the blood along the lymphatic channels from the tissues (Virchow, Cellularpathologie, IV. Auflage (1871). p 198), and appears to be a product of their activity, it seems reasonable to attribute the hypinosis to diminished energy of tissue metamorphosis. Whether the low degree of fibrinoplastic power exhibited by the blood be in any way connected with the oligocythæmia must for the present be left an open question. There are many grounds for thinking that it is. For, since the red corpuscles are very rich in fibrinoplastic matter (A. Schmidt, Kuehne), it does not seem far-fetched to suppose that the slow coagulation of anæmic blood may be connected with its poverty in colored elements. Against this view, of course, is the fact that wholly defibrinated serum still

retains an abundance of fibrinoplastic matter. Accordingly, the latter cannot be exclusively limited to the red corpuscles; it is present, in excess, in the plasma likewise. There is yet another fact in support of the view that the tardy coagulation of the blood depends on the oligocythæmia. We know that oxygen favors coagulation; that blood drawn from the vessels coagulates more quickly in proportion to the amount of oxyhæmoglobin it contains. Now, as the amount of hæmoglobin is diminished in anæmia, we may assign this as a cause of the impairment of the fibrinoplastic energy of the blood.

II. *Constitutional Symptoms.*

The constitutional symptoms of anæmia are of two kinds. Some are a direct result of the visible alterations in the state of the blood which have just been described. Others are due to the influence of the fundamental disorders, chiefly hypalbuminosis and oligocythæmia, which underlie those alterations and modify the nutrition of the entire organism, the molecular changes taking place in it, and the energy that it displays. Among the former may be enumerated the altered color and consistency of the skin and other parts, and the dropsical symptoms that are so often observed. Among the latter, the general emaciation of the body, the degenerative processes, the modifications in the income and expenditure of matter and energy (formation of urea, production of heat, etc.).

1. *Color and consistency* (“*turgor*”) *of the skin and other parts.*—The peculiar decoloration of the skin and visible mucous membranes which anæmic patients exhibit during life, and which, as we learn by post-mortem examination, is common to all the internal viscera as well, depends partly on the paleness of anæmic blood, partly on the small quantity of blood contained in the various organs, partly on their diminished “turgor.” The normal hue of the tissues depends in great measure on their vascularity, a definite proportion of blood-red being combined with the special tint of the tissue-elements. As the superadded redness is withdrawn, the color that is peculiar to every organ starts into greater distinctness. Again, the dimin-

ished "turgor" and collapse of the emptied vessels brings the tissue-elements into closer approximation; hence, any tissue which has a definite color of its own will manifest it not only in a more unmixed, but in a more intense form. These statements are admirably illustrated by the skin, which admits of being watched and studied during life. Not every one is rendered paler by anæmia; dark-complexioned persons and the dark-skinned races of mankind actually grow darker under its influence. This singular fact is readily explained by the considerations given above, as was pointed out by Hebra. The rule fails to hold good only when the anæmic skin of a dark-complexioned person happens at the same time to be œdematous. For the corium is then saturated with an all but colorless serum, and the pigmented elements of the *rete Malpighii* are separated from one another; hence, the surface grows inevitably paler. Anæmic patients with much dropsy (*e. g.*, those suffering from kidney disease with albuminuria) are always very pale, whether their skin happen to be loaded with pigment or not.

For the rest, it may be laid down as a rule that the decoloration of the skin and other parts in anæmia will be proportionate to the reduction in the total amount of blood in the body, and, more particularly, to the poverty of the fluid in red corpuscles. Hence, the most extreme degree of decoloration, during life and after death, occurs in anæmia after hemorrhage. The symptom is likewise well marked in those forms of the disease which are characterized by severe oligocythæmia, whether this be due to immediate damage inflicted on the corpuscles, as in protracted fevers, diseases of the spleen, etc., or be of a secondary kind—an element in advanced marasmus.

On the other hand, the diminished "turgor" of peripheral parts, which, as we have seen, contributes to modify their color, is exclusively due to the lessened amount of blood they contain. Hence, it is most marked when the total volume of blood in the body is greatly reduced, as it is in acute anæmia after hemorrhage; also in states of extreme inanition or excessive consumption (cancerous marasmus, hectic fever, etc.).

But it must not be forgotten that both the color and "turgor" of visible parts, since they depend solely on the amount of blood these parts contain, are liable to be modified, not merely by the color and abundance of the blood in the body, but also by the way in which it is distributed. But the latter is regulated by the heart's action and the tonus of the peripheral arterioles. We know how sanguine people turn pale, how their features shrink, when the heart's action is reduced to a minimum by syncope or nausea ; in much the same way the superficial vessels of anæmic persons are habitually rather empty, because their heart's action is always weak and not seldom inadequate. This cause must accordingly help to render their skin pale and to lessen its natural "turgor." On the other hand, even an anæmic subject will flush when the heart is temporarily excited, especially if the cutaneous arterioles are simultaneously relaxed so as to admit more blood. Inasmuch as the vaso-motor system is remarkably unstable in the majority of anæmic persons, they are eminently liable to partial fluxionary congestion of the skin from trifling causes. They blush easily under the influence of emotion.

2. *Dropsy.*—The dropsical symptoms whose predilection for certain forms of anæmia has already been alluded to, are chiefly due to the hypalbuminosis of the blood. I have already pointed out that the volume of the blood depends mainly on the amount of albumen in its plasma ; albumen having power to absorb water and incorporate it. Hence, the less albumen the blood contains the less water does it take up from the tissues—the smaller the proportion of the interstitial juices that finds its way by osmosis into the blood-stream. Accordingly, hypalbuminosis, when it has reached a certain point, inevitably causes stagnation in the interstices of the tissues, and thus give rise to œdema ; at a later period, large quantities of serum accumulate in the serous cavities (ascites, hydrothorax, etc.). The precise degree of hypalbuminosis requisite to produce dropsy cannot be definitely fixed ; for the quantity of fluid in the tissues does not depend merely on the proportion of albumen in the blood, but on the blood-pressure likewise. Hence, the statement of Becquerel and Rodier, that dropsy must ensue whenever the proportion of albuminates in the blood has fallen from about 8 per cent. to about 6 per cent., can no longer be accepted without qualification. It may safely be affirmed, however, that the

various causes of anæmia favor the development of a so-called "dropsical crasis" in proportion as they tend to induce a state of hypalbuminosis.

We are now able to understand how it is that severe albuminuria, or diarrhœa with great evacuation of albuminous matter or of peptones from the bowel, so frequently occasions severe dropsical symptoms; further, how it comes that a certain liability to dropsy is associated with nearly every form of anæmia.

But the actual circumstances are nearly always too complex to allow of our estimating the probability of dropsy, or foreseeing its degree of intensity, by exclusive reference to the supposed deficiency of albuminous matter in the blood. Suppose, *e. g.*, that we have reason to believe that the proportion of albumen in the plasma is abnormally small, while the total volume of the blood is greatly reduced. Under such conditions, we can scarcely anticipate any grave amount of dropsy, since, owing to the low pressure in the vascular system, very little fluid will be likely to transude from the blood into the tissues.

These conditions are actually realized during the febrile process. Notwithstanding extreme hypalbuminosis, dropsy is rare in fever, because a great amount of water is simultaneously eliminated through the lungs and skin.

But as any diminution in the aggregate amount of albumen contained in the blood is necessarily followed by the removal of a corresponding quantity of water through the emunctory organs, it is clear that no serious degree of dropsy can occur unless the hypalbuminosis be associated with actual hydræmia from interference with the elimination of water.

The terms "hypalbuminosis" and "hydræmia," though often employed indiscriminately, are by no means synonymous. The former denotes a primary diminution of the albuminates of the blood; the latter, a primary increase of the amount of water it contains. It is true that hypalbuminotic blood is *relatively* rich in water, hydræmic blood *relatively* poor in albumen; and so far as the phenomena of dropsy are susceptible of being explained by reference merely to the degree of concentration of the blood, the two expressions may be employed promiscuously. But this is not the case when, as in duty bound, we take the blood-pressure into consideration likewise. The latter depends, in a very considerable degree, on the total volume of the blood, as well as on the energy of the heart's action; but the total volume of the blood is increased in true hydræmia (from retention of water); hence, although the latter augments the quantity of fluid in the tissues and thereby tends to cause dropsy, the dropsy differs from that due to simple hypalbuminosis in being of an essentially *active* kind. But when a great drain of albumen happens to coincide with a retention of water in the system—when the two factors are at work together, as, *e. g.*, in many obstructive diseases of the kidney—then we may anticipate that dropsy will be developed very rapidly and will attain a high degree of intensity, and our anticipations will usually be fulfilled. Since, however, in most forms of anæmia, only one of the two factors, viz., hypalbuminosis, is in operation, the dropsy is generally limited to that slight œdema of the skin, and trifling effusion into the serous cavities, with which we are so familiar.

Lastly, the action of the heart has to do with the occurrence of dropsy in many cases of anæmia. When it is very feeble, the veins and capillaries become overloaded in contrast to the relative emptiness of the arterial system. Moreover, should the heart be unable to cope with the influence of gravity, venous stasis is very prone to occur in dependent parts (especially in the lower extremities, the genital organs, etc.). Thus a mechanical dropsy often becomes associated with that caused by the morbid condition of the blood; nay, there can be no doubt that slight œdema of the lower limbs in anæmic patients (*e. g.*, those convalescent from fever) is often due to persistent weakness of the heart, and fully merits the name of "*hydrops gravitativus*," by which it is familiarly known.

3. *The nutrition of the body* (marasmus, degenerative processes, hemorrhagic diathesis).—The various modifications experienced by the nutrition of the body during protracted anæmia may for the most part be summed up in the word "marasmus." The emaciation of the proper substance of the body or general atrophy of the tissues takes place with varying rapidity in the different forms of anæmia, and attains very various degrees of intensity, according to the character of the fundamental process which lies at the root of the anæmia. Loss of weight—beyond what can be accounted for by the diminished plethora of the parts—is the common and essential characteristic of all marasmus; the other tissue-changes, observed on microscopical examination of the various organs after death, are not exactly identical in all places. Putting aside the degenerative class of processes (to which we shall have to return farther on), and confining ourselves to the processes included under simple atrophy, we find, even within these narrow limits, the constituent elements of the different varieties of tissue presenting an appreciable diversity of morbid change. Take the atrophy of the adipose tissue—one of the most striking phenomena of marasmus. The loss of bulk is exclusively due to the disappearance of fat from the fat-cells, the cells themselves remaining intact. In other

kinds of tissue, again (*e. g.*, many gland-cells), it is the corpuscular protoplasm itself that suffers; or again (*e. g.*, in muscle), the shrinking of the individual elements is associated with a simultaneous and considerable reduction in their number. Accordingly, marasmus involves, now a simple loss of the accidental constituents of the cell, now a true wasting of the cell itself (diminution of the proper body of the cell), now a numerical atrophy, or, to speak more accurately, an *aplasia* (hypoplasia) of the tissues (Virchow). But all these structural alterations have one feature in common: they are all of a "retrograde" character, *i. e.*, they all tend to diminish the actual bulk of the organs. As regards their origin, moreover, they are traceable to a disturbance in the equilibrium of the economy—to a want of proportion between the consumption and renewal of the tissue-elements.

Marasmus, viewed as an anatomical unity no less than as the expression of a universal disorder of nutrition, may arise in consequence either of inanition or of consumption. In other words, that want of proportion between the consumption and the renewal of the tissues, which ends in a diminution of the bulk of organs, may be primarily due either to inadequate renewal or to excessive consumption. Now, anæmic marasmus—the marasmus developed as a constitutional symptom of anæmia—is invariably, as regards its pathogeny, due to inanition. In addition to this, however, an anæmic subject may not unfrequently become affected by that form of marasmus which depends on increased consumption; but the latter, in its relation to the blood-change, must always be viewed as an independent complication—as co-ordinate with, not consequent upon it.

If we consider all the possible ways in which an anæmic state of the blood, as such, may affect the processes of nutrition and growth going on in the organism, the proposition just laid down will be seen to be logically unavoidable. All that we know is in favor of the belief that the nutritive and plastic activities which constitute the life of the cell are intimately bound up with an absorption of albuminous compounds from the nutrient fluid. Hence, it follows that a state of persistent hypalbuminosis, such as that associated with most forms of anæmia, must inevitably reduce the tissue-elements, sooner or later, to smaller rations—must subject them to inanition. Again, the capability or tendency of the tissue-elements to draw nourishment from the blood depends, in no small measure, on their being supplied with the necessary vital stimulus by the oxygen of the red blood-corpuscles, so that the oligocythæmia of anæmic persons will also contribute to produce inanition and consequent marasmus (but *vide infra*). Accordingly, the effect of anæmia is always to reduce the tissues to a state of inanition; and this, when it lasts for any time, and is at all severe, leads in the manner just indicated to marasmus.

Notwithstanding what has just been said about the influence of oligocythæmia, there can be no question that hypalbuminosis is the most important of the fundamental changes in the blood as regards the causation of marasmus. For we know from experience that in the peculiar form of anæmia termed chlorosis, extreme oligocythæmia coexists with an almost entire absence of wasting; probably because, in this disease, the proportion of albumen in the blood is not markedly diminished. Again, in that form of anæmia which results from disease of the spleen and lymphatic glands, and which seems to be primarily an oligocythæmia, the marasmus is quite insignificant by the side of the extreme pallor of the patient (p. 351). On the other hand, it may be laid down as a rule that marasmus is most marked in those forms of anæmia where a protracted and severe hypalbuminosis is the primary change, oligocythæmia being subsequently associated with it (as a secondary phenomenon—as one of the constituent elements of the marasmus). This group includes most of the graver varieties of subacute and chronic oligæmia (excepting those above alluded to), concerning whose manifold pathogeny I have said enough in a previous section. But, even apart from the evidence drawn from experience, there are *à priori* grounds for assigning a secondary place to oligocythæmia among the efficient causes of anæmic marasmus; nay, even for viewing oligocythæmia as in some degree opposed to its development. Physiology teaches us that while the red corpuscles, as carriers of oxygen, in all likelihood stimulate the appetite of the tissue-elements for the pabulum contained in the blood, and thus promote assimilation, they also promote the consumption of the tissues—the decomposition of albumen, the oxidation of fatty matter, etc. Hence, while oligocythæmia may, on the one hand, interfere with nutrition and delay its progress, on the other it must tend to preserve the tissues, retarding, to some extent, their disappearance.

The febrile variety of anæmic marasmus occupies a very peculiar position; for its pathogeny is complex, *i. e.*, it is not wholly due to the febrile anæmia. Fever, indeed, illustrates the combination described above in general terms, viz., increased consumption going on together with inanition of the tissues. The latter is the only factor in the production of the febrile marasmus which is causally connected with the febrile anæmia; the increased consumption of tissue, on the other hand, being wholly independent of the anæmia, and peculiar to the febrile process itself. Inasmuch, moreover, as the latter is the principal cause of the marasmus, this assumes more of an independent and co-ordinate position in reference to the anæmia. This point, as the reader will no doubt remember, was kept in view by me when I attempted to trace febrile marasmus to its origin, in a former chapter (Etiology).

When speaking of the structural alterations resulting from anæmia, I took occasion to refer to the singular fact that the various tissues and organs do not lose weight uniformly, some parts wasting very rapidly, while others waste but little. Our knowledge on this subject is most precise in connection with that form of anæmia which results from inanition (in the narrower sense of the term)—from defective supply of food. By weighing the various tissues and organs of animals starved to death, Chossat has furnished us with the following scale of approximate values for the loss of weight that takes place:

	Loss of weight in hundredths of the normal average weight.
Adipose tissue	About 92 per cent.
Spleen	" 70 "
Liver and pancreas	" 50 "
Voluntary muscles	" 42 "
Heart and intestines	" 40 "
Kidneys	" 30 "
Lungs	" 20 "
Bones	" 16 "
Eyes	" 10 "
Brain and spinal cord	About 2.5 to 2 "

To go further into particulars, it was noted that those muscles which are kept most constantly at work (heart, muscles of respiration, and some others) are better preserved than the more inactive ones. Indeed, it may be affirmed, generally, that the degree of marasmus is proportionate to the functional importance—especially to the functional stability of the parts. This shows us that while the nutrition of the tissue-elements is, from the physical side, essential to the continued fulfilment of function, it is also, from the physiological side, dependent upon, and in some degree regulated by, functional activity. Parts whose functional activity is constant are better able to nourish and maintain themselves in time of need than parts whose activity is less pronounced; indeed, the latter would appear, by a sort of retrograde metamorphosis, to return some of their own stored-up pabulum into the blood, that it may serve to maintain the nutrition and functional activity of the former.

The degenerative processes so frequently associated with simple marasmus in anæmic states of the system demand a few words of notice. The reader may recollect that they consist principally in a fatty degeneration of the tissue-elements, in a retrograde metamorphosis of the albuminous tissues, which unquestionably points to their imperfect oxidation (Huppert, Senator, and others). These necrobiotic changes (Virchow) are especially marked when oligocythæmia is the primordial alteration in the blood (see chapters on Chlorosis, Progressive Pernicious Anæmia, Leukhæmia, and Pseudo-leukhæmia), or, at any rate, when a considerable diminution in the number of red corpuscles may be assumed to coexist with advanced hypalbuminosis (*e. g.*, in febrile anæmia, hemorrhagic anæmia, etc.). Hence, it does not seem in any way premature to regard the presence of fatty matter in or among dying tissue-elements as evidence of deficient oxidation, a result which manifests itself whenever, owing to a lack of oxygen-carriers (red corpuscles), the non-azotized products of the decomposition of albuminous substances by the molecular activity of the tissue-elements cannot be perfectly oxidized (into carbonic acid and water).

Finally, we have to consider the hemorrhagic diathesis which is not unfrequently developed in the more advanced stages of anæmia, notwithstanding the positive deficiency of blood. It is very closely connected with the altered composition of the blood, and often constitutes a true symptom of the anæmia. Recent investigations have shown that the normal function of the

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capillary walls—that of preventing extravasation of the blood *per diapedesin* or *per rhexin*—is inseparably connected with a normal condition of the circulating fluid. It is only by incessant renewal of the blood in contact with the capillary walls that the latter are enabled to fulfil their office, and even transient disturbance of the mutual relation between the blood and the vessels is enough, as Cohnheim[1] has experimentally proved, to produce changes in the vascular walls favorable to extravasation of blood. May we not conclude that an impoverishment of the blood, such as occurs in the more severe forms of anæmia, is capable of sometimes producing an effect upon the capillary walls similar to that produced by temporary arrest of their blood supply? The development of a hemorrhagic diathesis in many cases of anæmia may thus be classed with those constitutional symptoms, such as the marasmus and the degenerative processes, which result from the deteriorated nutrition of the body.

4. *Molecular metamorphosis and temperature.*—Just as a character of poverty and feebleness is stamped on the nutrition of anæmic persons, so also the flux of the vital processes, the molecular movement going on in the system, and the development of energy which is inseparably connected with it, are weak and sluggish. As regards the molecular changes that take place in the organism, this is proved by the quantity of the excreta. Anæmic persons, for the most part (*vide infra*), produce less urea, less urinary pigment (J. Vogel), and probably less carbonic acid (J. Bauer), than healthy subjects. Moreover, since the amount of actual excreta in anæmic persons is subnormal, we may conclude that the intermediate products of molecular metamorphosis—those which, containing a greater store of potential energy, are still capable of doing work in the system (*e. g.*, the specific constituents of the digestive juices)—are likewise formed in insufficient quantity and for too short a time. I have already pointed out how the so-called "atonic dyspepsia," present in very many cases of anæmia, tends still further to intensify the disorder. I have also made repeated allusion to

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[1] Untersuchungen über die embolischen Prozesse. Berlin, 1872. p. 28.

the detrimental influence exerted on the activity of the cytogenic organs by anæmia (spleen, lymphatic glands, marrow of bone, etc.), and manifesting itself by the production of a secondary oligocythæmia. The latter, by associating itself with the existing qualitative and quantitative imperfections of the blood, contributes, together with the consecutive hypalbuminosis due to the atony of the digestive apparatus, to give to many forms of anæmia the progressive character they exhibit.

All the above considerations become tolerably clear when we reflect that the energy of molecular metamorphosis, as a whole, and the functional activity of individual organs, depend in great measure on the amount of potential energy stored up in the circulating blood; but this is embodied in the totality of the functionally important constituents of the blood (especially in the red corpuscles, as oxygen-carriers, and in the chemically complex albuminates of the plasma), whose diminution is actually the characteristic and essential feature of anæmia. Accordingly, the activity of molecular movement must needs wane when the sources of energy (chemical affinity), drawn upon by the contact of the blood with the tissues, are gradually dried up in consequence of some defect in the composition of the nutrient fluid. I need hardly point out that, when anæmia is already present, the sluggish inadequacy of molecular metamorphosis will manifest itself most vividly whenever the introduction and assimilation of nutriment is hindered for any length of time either by internal or external causes—whenever, in other words, the anæmia has its source in inanition. It is the less necessary for me to insist on this fact, as the influence of inanition in reducing the quantity of the excreta—especially of urea—is a familiar and well-established physiological doctrine.

Whereas, in cases of the last-named kind, the effects of an existing anæmia may combine with those of chronic inanition to retard molecular metamorphosis, we find the two in direct antagonism to each other in the consumptive forms of anæmia. In the febrile variety of the disease, for instance, we have already learned that molecular metamorphosis is at first, while the pyrexia is predominant, greatly accelerated (as seen by the increased amount of urea, urinary pigment, carbonic acid, etc., eliminated); as time goes on, however, the influence of the pyrexia is more and more neutralized by that of the consecutive anæmia; and so it comes about that, notwithstanding the continuance of the febrile waste, the absolute quantity of urea formed, of carbonic acid eliminated (Leyden), etc., returns ultimately to its normal level, or may even sink below it; the energies to which molecular metamorphosis owes its principal impulse gradually subsiding more and more completely.

The effect of large bleedings on the activity of molecular metamorphosis may be alluded to in this connection, though it is worthy of notice on other grounds as well. The researches of J. Bauer have shown that in animals (dogs), during the first few days after a profuse hemorrhage, the amount of nitrogen eliminated is appreciably, though not excessively increased. Hence, we may infer that the decomposition of albumen in the body is somewhat augmented. The same observer found, moreover, that the elimination of carbonic acid, in contrast to that of nitrogen, is diminished. Now, Bauer is inclined to assume that, owing to the sudden removal of a considerable portion of the store-albumen of the blood (by venesection), a part of the more stable organ-albumen is converted into store-albumen and decomposed—that part of it, namely, for whose maintenance the store-albumen remaining in the blood is no longer adequate. This would explain the increased elimination of nitrogen. Again, Bauer supposes that the resulting oligocythæmia, by causing oxygen-starvation, hinders the non-azotized products of decomposition from being completely oxidized, and thus leads—first, to a diminished formation of carbonic acid; secondly, to fatty degeneration of the tissues. For details the reader may consult Bauer's own work (see *Bibliography*); for I cannot, on the present occasion, discuss the first part of the above hypothesis more fully.

A general survey of all that we know concerning the molecular metamorphosis, the nutritive and formative activities of anæmic persons, brings us to the conclusion that, a few peculiarities apart, the organic movement (or flux of vital processes), whether as regards the mass moved or the rate of its motion, is lessened in proportion to the degree of impoverishment of the blood. But the considerations enumerated above show that the activity of molecular metamorphosis in anæmic individuals is reduced because the diminution in the number of red corpuscles, in the amount of plasmatic albuminates, etc., entails a corresponding diminution in the store of potential chemical energy, to which the organic movement may be said to owe its very existence.

These views are further corroborated by what we know of the temperature of the body in anæmic patients. Since the greatest part of the energy developed in the organism is expended on the production of heat, we may assume that any decrease in the functionally important ("charged with potential energy") constituents of the blood will be followed by a diminution in the average amount of heat produced, the latter betraying itself by a tendency to low degrees of temperature. In point of fact, we *do* find the temperature of anæmic subjects usually rather low, often quite subnormal; and there is reason to ascribe this to lessened heat-production, since it cannot always be accounted for by increased dissipation of heat. It can only be attributed to the latter cause when a transient afflux of blood to the skin, or a profuse perspiration, immediately precedes an unusual fall of temperature. But we very often find the temperature of anæmic persons permanently low, and associated with a pale, dry skin; in such cases we cannot but think of lessened heat-production. The latter, too, will serve to explain the liability of anæmic persons to subjective sensations of cold, when the temperature of the air is by no means very low; though feebleness of the heart's action must contribute its share, by allowing the blood to stagnate in internal parts instead of pumping it to the surface. The skin thus contains too little arterial blood; it is insufficiently heated, and those nerve-ends by which we appreciate variations of temperature are stimulated just as they might be by actual coldness of the surrounding medium; hence the sensation of cold, exactly similar to that produced by the cutaneous anæmia resulting from spasm of arterioles.

In striking contrast to the subnormal temperature of many anæmic subjects stands the abnormally high temperature of febrile patients. This is chiefly due to increased heat-production from increased activity of molecular metamorphosis. The longer the fever lasts, however, the more marked does the antagonistic influence of the febrile anæmia become, and the more characteristic are the modifications that it introduces into the temperature curve due to the pyrexia itself. For, as the patient grows more and more anæmic, the continued type of his daily temperature is modified by remissions and finally by intermissions. Intercurrent collapse of the temperature, during which it may sink very low indeed (33° to 35° C. = 91.4° to 95° F.), sometimes occurs, either quite spontaneously, or as an unexpected result of trifling antipyretic measures (moderate withdrawal of heat, small doses of quinine, digitalis, etc.); it points to a reduction in the energy of the heat-producing processes, which prevails more and more over the pyrogenic cause. Nay, in well-marked forms of hectic (the fever of patients who are already anæmic), such as are seen in the last stages of phthisis, the pyrogenic matters resulting from the breaking-down of lung-tissue are at last no longer able to excite any appreciable rise of temperature or febrile movement. We then see the curve, after having exhibited during a variable period of time the familiar type of a quotidian intermittent, present that ominous fall of the evening temperature to a subfebrile or even normal level, which—so far from being a good sign—is usually the forerunner of death. We shall not often go wrong if, in the last stage of phthisis, we predict death in from 48 to 72 hours, when, without adequate apparent cause, the high level of the evening temperature (39°–40° C. = 102.2°–104° F.) sinks to 38° C. (100.4° F.) or lower, while the morning temperature at the same time falls to 36° C. (96.8° F.) or less.

Lastly, the depressing effect of severe oligæmia on the temperature of the body is also shown by the sudden and striking fall of temperature (of course, only transient) that commonly follows profuse hemorrhage occurring in the course of a febrile malady (*e. g.*, from the bowel in enteric fever). When the effused blood does not actually show itself till later, the fall of temperature is the first sign from which we learn that internal bleeding has taken place, and the physician who is armed with the thermometer thus receives timely warning of imminent, though hidden, danger.

Accordingly, we may regard it as established that just as anæmia restricts and inhibits the phenomena of oxidation and decomposition taking place in the system, so the energy set free in the form of heat by the chemistry of molecular metamorphosis undergoes a diminution. The same is true of the mechanical work done by anæmic persons; but, owing to its intimate connection with the muscular system, I prefer to discuss this branch of the subject in the ensuing section.

III.—*Local Symptoms.*

I cannot undertake an exhaustive analysis of all the local symptoms of anæmia on the present occasion—I have not enough space at my disposal; moreover, it is impossible, with our present knowledge, to subordinate *all* the phenomena in question to physiological laws. I shall therefore limit myself to a brief description of the symptoms connected with the more important organs, and to those more particularly which lend themselves most readily to physiological analysis. The symptoms presented by the muscular system deserve the first place, partly for the reason I have just given, partly because a consideration of the mechanical work done by anæmic subjects connects itself naturally with that discussion of their heat-producing powers with which the previous section concludes.

1. *Muscular system.*—"Muscular weakness" is the most striking feature presented by the voluntary (and involuntary) motor apparatus of anæmic persons. This term, however, is so often used to denote definite morbid states that it is desirable, in order to avoid all chance of misunderstanding, to define it precisely. The "muscular weakness" of anæmia shows itself, in a vast majority of all cases of the disease, as a "premature functional insufficiency" of the locomotor apparatus; in other words, as a "liability of the muscles to premature fatigue in consequence of mechanical exertion." But it rarely presents itself as an *absolute* feebleness of the muscles, *i. e.*, an inability to contract vigorously. It would be altogether a mistake to imagine that an anæmic subject is incapable of muscular effort—that the muscular tissue, in the graver forms of anæmia, loses the power of contracting vigorously, and of doing a relatively large amount of work in a short time. Any such notion would lead us astray at the very outset of our inquiry. Consider the violent convulsions that occur, both in man and in the lower animals, during fatal hemorrhage; convulsions which, though

coinciding with the most extreme anæmia, can hardly be taken to indicate any absolute functional insufficiency on the part of the muscular system. Consider the frantic violence of anæmic patients when delirious. Consider the many instances in which deadly peril or other urgent need has found even the weakly and anæmic able to display the strength of heroism or of despair. All this shows that anæmia is quite compatible, up to a certain point, with muscular energy. The chief difference between the muscular activity of anæmic and that of healthy persons consists in the want of staying power displayed by the former, a feature not to be confounded with absolute weakness of the muscles. While a healthy man is capable of severe and prolonged exertion, the muscular apparatus of one who is anæmic speedily gives in; moreover, it requires a much longer interval of rest to render it capable of fresh exertion. This liability to fatigue is obviously connected with the insufficiency of the chemical changes taking place in the muscles of anæmic subjects; the functional renewal of the wearied muscles takes place too slowly. On the other hand, the violent and unexpected outbursts of muscular energy in anæmic persons—such as occur after long periods of repose—furnish additional evidence in favor of the physiological doctrine that a muscle capable of doing work requires only a stimulus to throw it into a momentary state of vigorous contraction, and not a supply of blood as well; in other words, that it contains an intrinsic store of energy ready for discharge at any moment.

Looked at more closely, the following is probably the sequence of events: when a muscle contracts, a process of dissociation (analogous to that in fermentation), without any oxidation, takes place in its interior; energy is liberated, by means of which, under the influence of a stimulus (*e. g.*, of a volitional impulse transmitted through the motor nerves) the inogen contained in the muscle is split up into an albuminous body of smaller bulk (myosin), and certain non-azotized products (chiefly carbonic and sarcolactic acids). Hence, it follows that the muscles of anæmic persons are capable of vigorous momentary contraction under the influence of an adequate stimulus, provided they contain a sufficient store of inogen; and this they unquestionably do, both in acute anæmia after hemorrhage and in many other forms of anæmia likewise after prolonged repose.

But if a muscle be required to work for any length of time, its inogen must be continually renewed; for, as I have repeatedly pointed out, it splits up and is destroyed during every act of contraction. Its renewal is effected by the blood; the synthesis takes place in the interior of the muscle itself, which furnishes its residual myosin for the purpose, while the blood supplies oxygen and compounds containing carbon and hydrogen; no further provision of albumen being necessary. Now, if the composition of the blood be impaired, as it is in anæmic subjects —if there be any great degree of oligocythæmia—the functional renewal of the muscles, as the store of inogen is more and more exhausted by prolonged exertion, takes place but slowly and imperfectly, and premature fatigue sets in. There is yet another point of some importance to be noticed. The non-azotized products resulting from the decomposition of inogen (sarcolactic acid, carbonic acid, etc.) belong collectively to the class of so-called "fatiguing substances" (J. Ranke), whose presence and accumulation in the muscle hinder the further dissociation of inogen. Hence, the capacity for protracted exertion implies not merely an abundant synthesis and renewal of inogen, but also a simultaneous elimination of the "fatiguing substances" from the working muscle. This emunctory office is performed by the blood, which washes out the waste-products from the tissue. Should the circulation be sluggish (as we may assume that it is in many cases of anæmia, from the weakness of the heart's action and other signs of irregular distribution of the blood), the imperfect removal of waste-products will inevitably contribute to the premature exhaustion of the contractile tissue. More especially will it necessitate an interval of rest after any considerable exertion—an interval much longer than that required by the muscles of healthy persons for their renewal.

The above remarks show, in the first place, how far physiology can go in explaining the pathological phenomena of premature fatigue of the muscles; secondly, they enable us to account, on chemico-mechanical principles, for the momentary activity sometimes exhibited by anæmic persons. But when we go on to consider that state of real muscular weakness which is met with occasionally, and not very unfrequently, in certain special forms of anæmia, we find ourselves engaged on a more complicated problem. A number of causes appear to be at work together, and these causes are not always the same in all cases. In the first place, when severe anæmia has lasted for any time, the functional restoration of the muscles grows more and more imperfect; in many instances it wholly fails to compensate for the simultaneous expenditure of muscular power, to keep pace with the gradually increasing exhaustion; and thus a state of permanent weakness of the locomotor organs is induced. Next, there are the muscular atrophy and degeneration, which are never absent in the chronic forms of anæmia. The more advanced these changes are in any case, the more profoundly is the maximum working power of the muscles reduced—the greater the degree of absolute functional weakness superadded to the liability to premature fatigue. Besides the causes I have just enumerated, which reside in the muscular tissue itself, there can be no doubt that in many cases the nervous system exerts a depressant influence upon the working power of the muscles. For instance, a subjective feeling of weariness often prompts anæmic patients to restrict their movements voluntarily, so far as their muscles are under the control of the will; they exert themselves only in moments of emotional excitement, when the memory of former weariness, and the weariness already felt, are unlike unheeded. Lastly, motor innervation is itself impaired in severe anæmia. The centres of volition in the cortical substance of the hemispheres, the motor centres in the brain and cord, and the peripheral motor nerves, undergo serious functional disturbance in consequence of an insufficient supply of blood. The discharging forces requisite for the fulfilment of powerful muscular contractions are thus frequently inadequate, and the latter either do not take place at all, or take place feebly; not because muscular contractility is itself proportionately diminished, but because the muscles are no longer incited to vigorous contraction.

2. *Nervous system.*—Imperfect as is our knowledge of the chemical changes taking place in muscle, and of their relation to

the composition of the blood, it appears perfect in comparison with that which we possess concerning the nutritive processes going on in the nervous apparatus and their relation to the blood. Considering the slight vascularity of the peripheral nerve-trunks, we are justified in believing that the molecular changes going on in them are, quantitatively, but small; concerning their magnitude in the more vascular nerve-centres, especially the gray matter of the brain and cord, we are entirely destitute of precise information.

It is therefore quite impossible to refer the symptoms presented by the nervous system in anæmia to definite and familiar alterations in the molecular metamorphosis of the nervous matter. Our knowledge in this department remains purely empirical, even when the morbid phenomena have received a certain measure of theoretical elucidation by physiological experiment. We are sometimes able to associate particular disorders of nervous function with particular degrees of anæmia; but we have no means of ascertaining the intimate nature of their connection.

The state known as "irritable weakness" is the most general of the permanent anomalies exhibited by the nervous system of anæmic persons. Besides this state, which, as I have just said, involves the nervous system in its entirety, we have a number of symptoms of a more local and accidental character—symptoms for whose production certain accessory conditions are required. Among these conditions are: the intensity of the anæmia at the moment; the rate at which it has been developed; finally, such external or internal circumstances as are specially adapted to augment the existing anæmia of particular regions of the nervous system.

The clinical manifestation of "irritable weakness" consists in an abnormal excitability of the nervous organs, together with an unusual liability to speedy exhaustion after being stimulated. The diminished power of resisting stimulation, exhibited by the nervous matter of anæmic persons, shows itself in a great variety of ways, and gives rise to a great variety of symptoms: first, in the vast domain of sensibility (using the term in its widest sense), as a morbid hyperæsthesia of all parts endowed with feeling. Sensory impressions that are too feeble to be perceived as such by healthy persons, often produce an appreciable degree of central irritation in the anæmic, the irritation being generally associated with very considerable central irradiation. The latter may be inferred from the peculiar fact that the feelings of pleasure, displeasure, and pain, may be excited in the anæmic by sensory stimuli that are much too weak to excite those feelings in the healthy. As a general rule, sensations only continue to give pleasure to anæmic persons so long as they are extremely feeble in degree (hence their fondness for subdued light, hushed music, etc.); when the senses are more powerfully appealed to, though still in a measure quite incapable of causing pain to the healthy—nay, likely to increase their enjoyment (*e. g.*, brighter illumination, louder and more resonant music), the anæmic patient will not merely be conscious of an abnormal objective intensity in the phenomenon, but will complain of its producing a disagreeable, nay, sometimes even "painful," impression upon him. This hyperæsthesia and hyperalgesia are not limited to parts endowed with objective sensory perceptions—such as the organs of special sense, and the skin—but extend to the remaining parts of the body likewise, whose sensibility is less developed. Disagreeable sensations of a vague and indefinite kind arise in the interior of the body, and are referred by the patient, with more or less precision, to particular organs; also positive pain of various kinds and in various situations (headache, backache, enteralgia, etc.). It is highly probable, though incapable of proof, that many of these abnormal sensations are due to slight irritation of the sensory nerve-ends in internal organs by variations of blood-pressure, changes of position, etc.—sensations only reaching the consciousness when the excitability of the nervous system has been exalted by the altered state of the blood. The origin of true neuralgia in anæmic subjects ought, in all likelihood, to be explained in a similar way; though here, of course, the trifling lesion is probably situated in the trunk of the sensory nerve instead of in its peripheral distribution. The nerve-trunk, at some point in its course, is thrown into an unusual state of irritation. Finally, it is worthy of note, that the abnormal excitability of the sensory nerves in anæmic persons extends to the domain of the so-called "common sensations," *i. e.*, includes those differentiated sensations which are prone to occur in connection with peculiar physiological states of certain organs, or with abnormal relations of the organism to its environment. All the members of this group, such as the sense of muscular fatigue, of hunger, voluptuous sensations, nausea, giddiness, etc., are usually more readily and quickly excited in anæmic than in healthy persons, and are often very intense. Thus, the sense of muscular weariness speedily becomes exaggerated into painful exhaustion, hunger becomes ravenous, etc.

While the entire sensory tract is morbidly hyperæsthetic, and becomes the theatre of a protean multitude of phenomena due to irritation, it is of great importance to note that every irritation is quickly followed by a premature exhaustion of irritability. The essence of "irritable weakness" consists in these oscillations between the two extremes of irritation and depression. Thus there arises—principally in the domain of sensation—that protean aggregate of symptoms in which opposite extremes succeed each other so suddenly and unexpectedly that the bystander is tempted to accuse the patient of sheer caprice and exaggeration. For instance, when the sensory organs of an anæmic subject have been excited for any length of time, their abnormal sensibility is replaced by torpor; pain itself is usually paroxysmal, and is often followed by numbness; ravenous hunger passes, after a few mouthfuls, into a feeling of repletion, etc. It is interesting to observe how any considerable degree of fatigue and languor is immediately followed by a peculiar loss of sensibility in the muscles; the patient feels as if his limbs no longer belonged to him. Upon the whole, it is not too much to say that the symptoms of diminished excitability of the sensory organs are at least as numerous as those of abnormal irritability.

But the irritable weakness of anæmic persons is by no means confined to the sensory apparatus. It involves the motor and vaso-motor apparatus likewise. Increased reflex excitability of the muscles is very common, especially in anæmic women and children, whose nervous system is, even in health, more easily excited than that of men. Anæmic women, and sometimes anæmic men as well, present symptoms that are almost identical with those of hysteria—nay, that form a recognized variety of the disease (*see* Complications and Sequelæ). In anæmic children the tendency to spasm may even culminate in the general convulsions (eclampsia) known as "hydrocephaloid" (Marshall Hall). These alarming accidents usually set out from some sensory irritation that is propagated to the brain, whence, owing to the abnormal excitability of the nerve-centres, it is forthwith reflected over the entire motor and vaso-motor systems, giving rise to convulsions and (owing to vaso-motor ischæmia of the cerebral hemispheres) to loss of consciousness as well. Local signs of vascular spasm or relaxation—ischæmia or fluxionary congestion of the skin and other organs—are often met with in anæmic adults; they point unmistakably to the existence of a morbid excitability of the vaso-motor apparatus. Lastly, I must once more allude to the psychical condition of anæmic patients. This, too, exhibits the characteristics of irritable weakness. Are not the exaggerated susceptibility of the emotions, the tendency to outbursts of feeling, passing from the extreme of vivacity and passionate endeavor to that of complete apathy and failure of will, the capricious temper changing with each varying mood—are they not all unmistakable signs of a morbid susceptibility of the nerve-centres? Is not the violence of the excitement—like the flame of burning straw which shoots up and as suddenly subsides—essentially momentary and lacking in persistency? The temperament of most anæmic persons may be set down as more or less decidedly "sanguine." There is something of irony in the circumstance that their psychical condition should be denoted by a term derived from that very liquid to a want of which the abnormal state of their emotional nature is chiefly due.

If we go on to inquire, after this brief summary of the symptoms, into the nature of the connection between the irritable weakness of the nervous system and the anæmia, we shall find ourselves driven to acknowledge that the causal relation between the two sets of pathological phenomena must remain for the present an ultimate fact of experience, which eludes any attempt to place it on a secure theoretical basis. So long as the chemical changes taking place in the nerves (during activity or repose) and the molecular forces concerned in their production are as good as unknown, it must remain impossible to construct any physico-chemical theory of "irritable weakness," and to deduce it as an inevitable consequence from the anæmia. Such statements as, *e. g.*, "that the insufficiency of the nutritive processes in anæmic persons gives rise to an abnormal want of stability in the chemical state of the nervous matter, thereby rendering it more prone to pass into the altered molecular condition known as 'excitement' under the influence of stimuli," are really no more than alternative definitions of the state of abnormal excitability itself. Still, they may serve to bring the mechanical side of the phenomenon before the mind and thus enable us to look deeper into its essential nature. Let us consider the analogy that exists—as shown by physiological experiments—between the behavior of the nervous matter in the irritable weakness of anæmia and the behavior of the nerves in course of death; in either case the final extinction of irritability is preceded by an immense exaggeration of it. We might even go on to affirm that the ill-nourished nervous apparatus of anæmic persons is permanently reduced to a state of lowered vitality or imminent death. This definition would include both the increased irritability of the nervous system and its liability to become speedily exhausted. The latter, indeed, is more amenable to theoretical explanation than the former; hence, its origin admits, to a certain extent, of being analyzed in conformity with actual facts and with the premises indicated above. If we regard it as certain that the consumption of the potential energy stored up in the nervous matter is proportionate to the frequency with which fractions of it are converted into external molecular work, and to the magnitude of those fractions (*i. e.*, to the frequency with which the nervous matter is actually excited, and to the excess of the excitement produced over the intensity of the exciting stimulus), we may view the facility with which the nervous energy of anæmic persons is exhausted as an inevitable consequence of the morbid excitability of the nervous apparatus, owing to which it is thrown into a state of actual excitement by a variety of stimuli, with unwonted frequency and unwonted severity. Inasmuch, moreover, as the original store of potential energy in the nervous tissue, owing to defective nutrition, may be supposed to be under the normal standard; inasmuch, further, as the renewal of the said energy when exhausted must take place slowly and with difficulty, we can readily understand why the nervous system of anæmic persons should give in so quickly and be so constantly in danger of functional exhaustion. This danger is greatly increased by the proclivity of the nervous system in anæmia to squander its slender stock of energy on every possible occasion, in explosive outbursts (as it were, to fire away all its powder in blank cartridges).

Irritable weakness, as a regular attendant on and consequence of the anæmic state, is obviously no more than a morbid tendency of the nervous matter; it is not in itself a pathological phenomenon. In order that irritable weakness may manifest itself objectively, some special impulse is always necessary. This enables the abnormal state to display itself clinically in the form of particular local symptoms. From this point of view the anæmia presents itself as the actual cause of the irritable weakness, but not as the exciting (discharging) cause of the nervous symptoms described above. It favors their occurrence, but is not of itself competent to produce them. But there are some local nervous symptoms of anæmia which stand in quite a different position. They are a direct result of the bloodlessness of definite portions of the nervous apparatus, particularly of the brain. So far as *they* are concerned, the accessory (discharging) factors alluded to above fall into the background among the predisposing causes. In order, however, that these neurotic local symptoms of anæmia may be developed, it is essential that the general anæmia should be severe, or that the local bloodlessness of particular parts of the nerve-centres should be rapidly induced. Hence, their occurrence is promoted by such conditions as raise the existing anæmia of the nervous organs to a high degree of intensity *gradually*, or else increase it to a more moderate extent *suddenly*.

It may be laid down as a general principle that local oligæmia, when of great intensity, soon annuls the irritability of the nervous matter. Sometimes, however, the symptoms of neuropathic paralysis are preceded by signs of violent irritation of those very parts of the nervous system which are about to surrender their functional vitality. Under favorable circumstances the irritation may subside without going on to paralysis. On the other hand, symptoms of paresis may be developed without evidence of antecedent irritation, and they may even culminate in complete paralysis sooner or later, if the local oligæmia go on increasing. It is a singular fact that certain parts of the central nervous system only exhibit signs of intense irritation when general anæmia comes on very rapidly, or when local anæmia is suddenly and greatly exaggerated; while other parts, on the contrary, undergo immediate paralysis when the anæmia is acute, and only pass through a previous stage of irritation when the anæmia is more gradually developed. Among the former are certain parts at the base of the brain; among the latter, the cerebral hemispheres stand foremost. The immediate cause of the phenomena appears to be the same in all cases, viz., the sudden or gradual arrest of the supply of oxygen—a gas that is essential to normal innervation.

Of the localized phenomena of anæmia, the following deserve to be individually analyzed:

a. *General epileptiform convulsions* (epileptoid fits, anæmic or suffocative convulsions). These are only met with in the most severe forms of acute general anæmia, and are usually the immediate forerunners of death. When the anæmia is slowly and gradually developed, they are either absent altogether, or they are represented by feeble twitchings ("Todeszuckungen") during the last moments of life. General convulsions are well known to break out in animals which are being bled to death slowly, before the fatal issue. They may also be produced by stopping the supply of arterial blood to the brain (Kussmaul and Tenner, Astley Cooper, and others), either by compressing or by tying the great arteries going to the head. Hence, the epileptic symptoms in acute general anæmia must be referred to sudden bloodlessness of particular portions of the motor tract, which are thrown into a state of intense excitement by being suddenly deprived of oxygen. The particular centre from which the general convulsions are "discharged" is probably the *pons Varolii* (Nothnagel). Owing to the severe dyspnœa by which the convulsions are invariably preceded it is impossible to decide whether the "convulsion centre" ("Krampfcentrum") in the *pons* is directly stimulated by the want of oxygen, or whether the violent irritation of the neighboring respiratory centres in the *medulla oblongata* may not be propagated by irradiation to the motor centres in the *pons*. Again, it may be asked whether the "discharging stimulus" for the intense dyspnœa and suffocative convulsions is the actual lack of oxygen, or the accumulation of poisonous products of retrograde metamorphosis in the blood (A. Schmidt, Pflueger), whose further oxidation is prevented by the lack of oxygen in question. Since intense irritation of those centres only occurs when the supply of oxygen is suddenly and quickly checked, and since this is the only condition under which any considerable accumulation of waste products in the blood can be supposed to take place, the latter of the above hypotheses seems the more likely one of the two. The former would fail to explain why it is that neither convulsions nor dyspnœa, but only progressive motor paralysis, occur when the brain is deprived of oxygen very gradually. In any event, however, the outbreak of general convulsions during acute anæmia from hemorrhage must be viewed as a result of the acute bloodlessness of the above-named parts of the brain—a result which invariably ensues, apart from the presence of any subsidiary conditions, whenever that primary condition is fulfilled.

We are not justified in regarding the so-called "suffocative" convulsions as etiologically identical with the eclampsia previously referred to in connection with the hydrocephaloid disease of children. The latter is peculiar to childhood; it may be developed, together with other signs of irritable weakness, as an exaggeration of reflex excitability, even when the anæmia is by no means extreme, and when it comes on gradually. The blood-change and the patient's time of life combine to predispose the system to such paroxysms of eclampsia, the actual paroxysm requiring certain additional factors (which may be of various kinds) for its production. True suffocative convulsions, on the other hand, are independent of age, sex, and constitution; they invariably break out when the supply of oxygen to certain regions of the brain is suddenly reduced to a minimum, or wholly stopped. Accordingly, though the eclamptic paroxysms of anæmic children are always serious, they have none of the fatal significance of suffocative convulsions, for the cause to which they are due is of a less malignant kind.

b. *Attacks of hiccough, retching, and vomiting.*—These are not uncommon in the more severe forms of general anæmia. They must be attributed to irritation of certain groups of muscles (the diaphragm, the muscles of the larynx, the muscles of the abdomen), the irritation being propagated from the nerve-centres. Though it is probable that these co-ordinated, involuntary, muscular movements are discharged from certain portions of the hind-brain, particularly the *medulla oblongata*, yet the precise starting-point of the impulses, especially of that which excites vomiting, has not yet been exactly determined.

c. *Delirium.*—This is chiefly observed in the subacute and chronic forms of anæmia as the delirium of inanition or collapse. It is usually of a maniacal character. Severe febrile maladies, after the actual pyrexia has subsided, often leave a state of extreme anæmia behind them, during which violent psychical disturbances are prone to occur. They are not unfrequently met with, moreover, at the approach of death from protracted and exhausting diseases. Finally, they have been observed in persons previously healthy as a symptom of idiopathic anæmia from inanition. The fact that the active cerebral excitement soon passes into stupor in fatal cases of anæmia renders it probable that it originates in an anæmic condition of the *cortex cerebri*, insufficient in degree to cause immediate loss of consciousness, *i. e.*, functional paralysis of the gray matter.

d. *Attacks of unconsciousness.*—These are extremely common in anæmia due to loss of blood; but they also occur in other forms of anæmia, as more or less important, and by no means unusual episodes in the course of the disease. They undoubtedly signify that the functions of the cerebral cortex are temporarily abolished, owing to extreme arterial anæmia of that part of the brain. Hence, it is clear that while the more extreme forms of general anæmia will often be sufficient, of themselves, to annul the functional activity of the gray matter, unconsciousness will also be produced, even when the general anæmia is moderate in degree, by any such accident as is calculated to lessen the supply of blood to the brain. The majority of these attacks may legitimately be included under the head of "syncope;" for their immediate cause is, as a rule, a momentary enfeeblement of the heart. Anything calculated to fatigue the cardiac muscle or to paralyze its movements (*e. g.*, violent exertion, depressing emotions, etc.) may bring on an attack. It is also clear that the erect posture must favor cerebral anæmia, and contribute to bring on syncope when the heart is weak; for gravity exerts an influence upon the distribution of the blood, and hinders its access to the brain. Hence it is that anæmic patients are very prone to feel faint or actually to faint away when they have been standing for any length of time; hence, too, in the graver forms of oligæmia, loss of consciousness may be induced by raising the patient up in bed, or allowing him to lie with his head too high. Finally, it is quite possible that the cerebral anæmia and resulting loss of consciousness may often be of an ischæmic character, due to over-stimulation of the vaso-motor centre. This is probably the mechanism of the loss of consciousness in the eclampsia of anæmic children suffering from "hydrocephaloid" disease. It is probable, too, that a sudden ischæmia coincides with the violent clonic spasm of all the voluntary muscles in the suffocative variety of convulsions.

We shall have occasion to consider several other nervous symptoms of anæmia, specially connected with particular physiological apparatuses, in the course of the following pages.

3. *Circulatory system.*—The circulatory symptoms associated with acute and chronic oligæmia are specially worthy of notice from a clinical point of view, for two distinct reasons. In the first place, they arise—together with the changes in the blood that are characteristic of anæmia, and to which they are themselves, for the most part, due—as the starting-point of a number of other symptoms both general and local, and determine the general course of the disease. Secondly, they furnish the most important diagnostic signs—apart from those furnished by the patient's outward aspect—of the presence of anæmia. I shall begin by giving a short account of the most prominent functional disturbances of the heart in anæmic patients; I shall then enter on a detailed consideration of those circulatory symptoms to which we are in the habit of ascribing a high degree of importance in the diagnosis of anæmia.

The action of the heart in anæmia differs in two ways from its action in health. First, its individual contractions are more feeble; we infer this from the weak impulse, the muffled sounds, the small and compressible pulse—we call it "simple or permanent feebleness of the heart." Secondly, the organ is very easily excited by all sorts of internal and external causes; it is subject to "irritable weakness." This manifests itself by the varying frequency of the pulse and the occurrence of paroxysmal attacks, during which a subjective sense of palpitation is associated with tumultuous vehemence of the heart's contractions. Both sets of symptoms—those of "simple or permanent" and those of "irritable" weakness—admit of easy explanation if we reflect, in the first place, that the heart as a muscular organ must take part in the functional and nutritive troubles that affect the entire muscular system; secondly, that its innervation, like that of other organs, shares in the "irritable weakness" of the whole nervous apparatus. Accordingly, the cardiac symptoms of anæmia may be viewed as a particular case—as a local expression—of constitutional changes that have already been described, and need not therefore take up much more of our attention.

The habitual feebleness of the heart in anæmic patients is chiefly due, in recent cases, to the inadequate functional renewal of the unresting cardiac muscle. When the oligæmia has lasted for any time, the gradual atrophy and degeneration of the muscular tissue tend to produce the same result. Nervous influences, too, may be at work; influences which, in some ill-understood way, regulate the average amount of excito-motor innervation so as to make it correspond with the store of available energy in each particular case, and thus prevent the heart from becoming too rapidly exhausted. At any rate, physiological experiments have made it likely that the measure of cardiac energy expended in a given time is usually proportionate to the requirements and capabilities of the organism at the moment; the state of the body as a whole, and the heart's action, being in intimate correlation, probably through the medium of the cardiac nerves.

Among the effects of the "simple or permanent" form of cardiac weakness, circulatory disturbances occupy a foremost place. They are very common in anæmic persons, and contribute, together with the original defect in the quantity and composition of the blood, to produce many of the symptoms of the disease. They consist in a relative over-distention of the pulmonary and systemic veins at the expense of the arteries, which gradually become less and less adequately filled; further, in a proclivity of the blood to gravitate to dependent parts; lastly, in a slowing of the entire current of the circulation. Hence, anæmic persons, notwithstanding the diminished volume of their blood, often show signs of venous stasis in dependent parts, due to the joint influence of cardiac weakness and gravity. These symptoms are known, from their mode of origin, as hypostatic congestion and œdema—"hydrops gravitativus." The tendency to passive congestion may become serious in the respiratory organs, where, by causing pulmonary œdema, it may assume the significance of a terminal complication. Again, the slowness of the blood-stream often permits spontaneous coagulation to occur; this explains the so-called "marasmic thrombosis," principally observed in the lower extremities, which exposes the organism to the risk of subsequent embolism. Accordingly, the habitual feebleness of the heart in anæmic persons is the source of a variety of secondary disorders, some of which present a high degree of prognostic importance, since, by implicating vital organs, they may place the patient's life in peril.

While the above symptoms of cardiac weakness, with its possible consequences (irregular distribution of the blood, evidence of retarded circulation) are permanently displayed by anæmic patients under ordinary conditions, the signs of irritable weakness alluded to above may rather be said to occur as accidental episodes in the course of the disease; they may, however, under peculiar circumstances, assume so predominant a degree of importance as entirely to modify, for a time, its usual character. The heart is far more irritable in anæmic than in healthy persons. The former are extraordinarily liable to attacks of palpitation (cardio-palmus, cardiogmus), during which the heart's contractions are abnormally rapid and powerful; they usually last for only a short time. Instead of the feeble or imperceptible impulse to which we are accustomed, we feel a diffuse pulsation all over the precordial region; the apex-beat is strong, perhaps even heaving; the pulse in the arteries is fuller, the carotids throb, and the usual paleness of the skin is masked by a vivid flush. Such attacks occasionally come on without apparent provocation; in most instances, however, they are brought on by various causes which tend to excite the heart even in healthy persons (bodily exertion, emotional influences, etc.). But whereas in the latter the exciting cause must be very powerful in order to produce a physiological erethism of the heart, and to modify the habitual uniformity of its action, in anæmic subjects the smallest exertion, the most trifling disturbance of the temper, suffices to throw the heart into a state of excitement, and to spur the pulse into a gallop. There can hardly be a doubt that this cardiac erethism is of nervous origin. Owing to the increased excitability of the entire nervous system, in which the excito-motor nerves of the heart are implicated, a variety of trifling or barely perceptible influences (not always those mentioned above) are able to produce a powerful effect upon the movements of the heart. The difference between the excitability of the heart in anæmic and in healthy persons is in degree only, not in kind; it probably concerns, not the mutual relations of the cardiac muscle and the cardiac nerves, but the latter alone. For it is only because the irritable nerves of an anæmic subject transmit more frequent and more powerful impulses to the cardiac muscle, that the latter's contractions momentarily become vehement and tumultuous—not at all because the cardiac muscle is itself more irritable. Hence, we may conclude that the cardiac erethism of anæmia forms one of the group of symptoms previously referred to as indicating abnormal irritability of the motor nervous apparatus.

But the general irritability is not confined to the motor nerves; it involves the sensory system likewise, and with it the heart itself as a sensitive organ. We all know that when the heart is greatly excited in healthy persons, whether by exertion, emotion, or otherwise, the objective phenomena of exaggerated pulsation are associated with a subjective sense of palpitation, oppression, and anxiety. Exactly the same occurs in anæmic subjects, only with a far higher degree of intensity. The patient feels as though his heart were about to burst through the walls of the chest; and although there is a simultaneous increase in the objective vehemence of the heart's action, yet we are often able to detect a contrast between the absolute intensity of the heart's contractions and the disproportionately tormenting sensations of the patient. Hence, we may fairly conclude that the sense of violent palpitation experienced by anæmic persons is not entirely due to the actual over-action of the heart during the paroxysm, but that there is cardiac hyperæsthesia as well—a hyperæsthesia analogous to the feeling of weariness in voluntary muscles and to exaggerated common sensations of other kinds.

The phenomenon I have just described, like the feeling of palpitation in a healthy person, appears really to be a subjective symptom of cardiac fatigue. At any rate, the subjective consciousness of over-action does not arise in health (when the blood and the muscular tissue of the heart are both in a normal state), except when the heart is actually forced to do a disproportionate amount of work in a limited time—in other words, to overwork itself. When the heart is hypertrophied, its action may continue to be objectively increased to an extent perfectly colossal for years together, without the patient making any complaint of palpitation. Cases of insufficiency of the aortic valves furnish most instructive instances of this fact.

The speedy and invariable occurrence of exhaustion — of cardiac paresis—after anæmic palpitation, scarcely requires to be explained. Not only must the motor innervation of the heart begin to fail when the slender store of energy in the excito-motor nerves is rapidly diminished without being adequately restored by the blood, but the cardiac muscle itself must soon lose the power of contracting as vigorously and as rapidly as it did during the paroxysm. The commencing failure of the heart manifests itself by symptoms which contrast in some degree with those described above. The energy of the contractions sinks to a minimum. Their frequency generally remains abnormally great, though irregularity and intermission may occur. The arteries are emptied, while the veins of the neck become distended, and the lips and cheeks grow cyanotic. The absolute præcordial dullness, as defined by percussion, is often found to be moderately increased in area. This is due to transient dilatation of the heart, whose ventricles are unable to empty themselves completely. The anæmic or accidental murmurs, to be described hereafter, are unusually loud, and are heard over an unusually extensive area. The feeling of palpitation persists throughout the whole of this period, and severe dyspnœa is also complained of. The patient may, perhaps, become unconscious, owing to a sudden attack of syncope, which may end either in recovery or in death. In the majority of instances, however, the cardiac paresis stops short of actual paralysis. After the symptoms have reached a certain degree of intensity, they usually subside, and the circulation returns to its habitual state until a fresh paroxysm occurs. We thus see that the function of the heart exhibits very manifold and characteristic forms of disturbance, more or less clinically important, in anæmic patients; and, though we are at present unable to furnish an exhaustive analysis of all the factors concerned in their production, an attempt has been made to show that the pathological phenomena admit of being subordinated to the general principles of physiology.

Two symptoms often met with in anæmic patients are worthy of special notice on account of their importance in relation to diagnosis. They are supposed, not altogether unjustly, to furnish valuable evidence of the presence of anæmia. I refer to the so-called "anæmic murmurs" audible over the region of the heart, and the "bruit de diable" heard in the veins of the neck.

The murmurs so frequently observed on auscultation of the heart in anæmic subjects, and termed "inorganic," "accidental," or "anæmic" murmurs, to distinguish them from those due to actual insufficiency of the valves ("organic" murmurs), do not differ in quality, or differ but slightly, from endocardial murmurs of the latter kind; for, although it is true that anæmic murmurs hardly ever display the rougher quality ("snoring" and "whistling") occasionally met with in those due to valvular disease, being usually soft and blowing, still, the latter qualities are by no means confined to the anæmic variety of murmur, but are very common in organic murmurs likewise. Further, it would be a mistake to suppose that accidental murmurs are necessarily gentle; under certain conditions—*e. g.*, when the heart's action is much excited—they may for a time be very loud, and audible over a large area. On the other hand, the great variations in their degree of loudness are undoubtedly characteristic. They are frequently heard only after the patient has been exerting himself, or when his heart is excited from some other cause, becoming once more inaudible during repose; but even this character is not decisive; it is frequently exhibited by murmurs which undoubtedly originate in defects of the valvular apparatus; and, on the other hand, many anæmic murmurs continue to be audible even when the patient is at rest. A leading peculiarity of accidental murmurs is that they are always systolic in rhythm; further, that, as regards their point of maximum intensity, they correspond precisely to those murmurs which are due to insufficiency of the auriculo-ventricular valves. Here we come across a difference between those accidental murmurs which are paroxysmal—only heard during cardiac erethism—and those which continue to be audible when the heart is tranquil. The latter are usually most distinct at the heart's apex, less commonly over the pulmonary orifice (second intercostal space on the left side); they are scarcely ever heard at the points where aortic and tricuspid murmurs are loudest. Hence, we may conclude that they are generated in the mitral orifice, and this conclusion may legitimately be extended to the cases in which the murmur is more distinct over the pulmonary artery than at the actual apex, since, as Naunyn[1] has shown, a slight increase in the length of the left auricle occasionally facilitates the propagation of sounds generated in the mitral orifice in that direction. On the other hand, when the accidental murmurs are only audible during cardiac excitement, they do not admit of being so precisely localized. They usually appear to be equally loud over the sternum and at the apex—a fact consistent with the view that they are generated simultaneously in both auriculo-ventricular orifices (cf. *infra*). Finally, there is one other point to be mentioned concerning anæmic murmurs of either kind; they are never associated, like the murmurs due to valvular disease, with the physical signs of compensatory hypertrophy of particular regions of the heart. This is the chief character on which we rely in deciding whether a given systolic murmur be of accidental origin or a sign of valvular mischief.

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[1] Berlin. klin. Wochenschrift. 1868. No. 17.

The following is probably the way in which cardiac murmurs originate in anæmic persons. Owing to the altered state of the blood, the muscular tissue of the heart is easily fatigued; and this liability to premature fatigue extends to the papillary muscles connected with the auriculo-ventricular valves. After any undue exertion on the part of the cardiac muscle, a temporary paresis of the *musculi papillares* ensues. In consequence of this the valve-flaps intrude into the auricles with every ventricular contraction; *i. e.*, a transient functional insufficiency of the tricuspid and mitral valves is established, and gives rise to a systolic murmur in the corresponding orifices. These murmurs only continue audible so long as the state of cardiac weakness lasts. As the organ regains its normal energy they grow fainter and disappear. In marked contrast to these intermittent murmurs, which are immediately connected with the paroxysms of cardiac excitement, the constant murmurs, usually limited to the apex, must be viewed as evidence of a persistent functional insufficiency of the mitral valves. They are probably due to permanent changes in the *musculi papillares* of the left ventricle, such as atrophy and partial fatty degeneration, to which this portion of the cardiac muscle is pre-eminently liable, and which are not unfrequently found to exist on post-mortem examination (Friedreich[1]). We may reasonably ask why the prolonged functional insufficiency of the mitral valve, such as appears actually to result from paresis of the *musculi papillares* in patients suffering from anæmia and marasmus, should not be followed by hypertrophy of the right heart, like that which follows the ordinary valvular insufficiency due to endocarditis. The answer to this inquiry is furnished by a consideration of various circumstances that are diametrically opposed to the development of the consecutive hypertrophy. First, the volume of the blood is diminished, so that the pulmonary circulation is never greatly overloaded. Next, the degree of valvular insufficiency is slight, for the valve-flaps are not shortened; their free edges are merely folded over into the cavity of the auricle. Lastly, the existing hypalbuminosis and oligocythæmia are obviously unfavorable to any secondary hypertrophy of the heart for the same reasons which make them give rise to atrophy and degeneration of its muscular tissue.

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[1] Handbuch der spec. Path. und Therapie, herausg. von R. Virchow. Bd. III. 2 (II. Aufl. 1867). S. 86.

The above explanation of the way in which anæmic murmurs originate seems to agree better than any other with clinical facts. The notion that the murmurs are a direct result of the watery condition of the blood has long since been abandoned; and there seems to be just as little ground for ascribing them—as is often done—to irregular vibration of the auriculo-ventricular valves. The latter view is unsupported by any positive evidence, while the fact that accidental murmurs closely resemble some of those caused by undoubted valvular mischief tells decidedly against it. Hence, we are driven to adopt, for the explanation of anæmic murmurs, the very same "hydraulic" theory which is now generally received as explanatory of the murmurs due to organic valvular mischief.

There is another reason (besides those alluded to above) for believing that in acute fatigue of the heart tricuspid insufficiency is often associated with functional incompetence of the mitral valve. It is this. At the height of a paroxysm of palpitation, the jugular veins may occasionally be seen to pulsate. The pulsation may be limited to the bulbar enlargement at their lower end, or it may be general. As the pulsation disappears after the attack, it may fairly be ascribed to a transient functional disorder of the *musculi papillares* in the right heart, due to fatigue, and causing temporary insufficiency of the tricuspid valve with regurgitation of blood from the right ventricle into the systemic veins.

Let us now consider the "bruit de diable" (*Nonnengeräusch*). This murmur, whose mode of origin has been the subject of endless discussion, is often, but by no means always, observed in anæmic patients. It was originally called by Laënnec "chant des artères"; he believed it to occur in the carotids. The term "bruit de diable" we owe to Bouillaud; the German name, "Nonnengeräusch," to Skoda. They are both derived from a well-known toy—the humming-top—known among the French as "diable," among the Austrians as "Nonne." The murmur in question is a continuous humming or rushing sound, periodically intensified by deep inspiration; it is heard over the internal jugular veins; it is usually louder on the right than on the left side, loudest over the jugular bulb and just above it. The murmur is momentarily arrested by forced expiration, coughing, straining, etc., but it always returns during the ensuing inspiration. It is better heard in the standing or sitting than in the recumbent posture. When very intense, it may be felt as a thrill by the fingers gently applied over the jugular bulb. The received theory concerning its mode of origin is that of Hamernyk. He believes it to be produced by a whirling movement of the blood in the jugular bulb, at the lower end of the internal jugular veins. For, as this portion of the vessel, situated just behind the sterno-clavicular joint, is firmly fixed on all sides, its walls are unable to collapse—like the walls of other veins—when the quantity of blood in its interior is diminished. Hence it forms a chamber, whose dimensions are constant, and largely exceed those of the vein immediately above it whenever the latter happens to be imperfectly distended, owing to a general or local deficiency of blood. Now, a stream of liquid flowing with sufficient velocity through a closed tube always forms a whirlpool when it passes abruptly from a narrower to a wider segment of the tube (Th. Weber); and its whirling movement, when sufficiently intense, is audible as a hydraulic murmur. In general anæmia, for the reasons already assigned, all the conditions required for the production of a constant hum are united at this particular point of the circulatory apparatus. The suction power of the lungs, moreover, is an auxiliary agent; by generating a partial vacuum in the interior of the thorax it accelerates the downward rush of blood in the lower part of the jugular veins, and draws the blood with great force into the veins of the chest. As the intrathoracic pressure sinks during inspiration, the venous hum grows more intense; it becomes feebler during ordinary expiration; while, in forced expiration (*e. g.*, during straining efforts), the increase of pressure in the chest prevents the blood from passing from the jugular into the intrathoracic veins, and the hum becomes inaudible. Finally, the increased distinctness of the murmur when the patient is in the standing or sitting posture is easily accounted for by the influence of gravity in promoting the flow of blood into the chest. Thus we see that, although there really is a causal connection between the venous murmur and an anæmic state of the blood, the connection is too indirect to allow of our regarding the murmur as pathognomonic of the disease. Still, when present, it proves that the veins of the neck are relatively empty, and that no obstacle exists to the entrance of venous blood into the chest—conditions most likely to be realized in severe anæmia unattended by disease of the respiratory or circulatory organs. Lastly, the student may be reminded that he ought not to press too firmly with his stethoscope when examining the veins of the neck; firm pressure will generate an artificial murmur in healthy subjects by narrowing the calibre of the vein. Another source of fallacy consists in forced rotation of the head to the opposite side; the jugular vein is then compressed, about its middle, by the tense cervical fascia and the belly of the omohyoid. Hence, a real murmur can only be affirmed to exist when it is heard at the point already indicated in a patient who holds his head straight, and with the stethoscope lightly applied. The phenomenon itself is not of sufficient clinical importance to justify discussion of the various other theories devised to account for it. The reader who desires further information will find it in works devoted to physical diagnosis.

4. *Organs of respiration.*—Dyspnœa is one of the most important symptoms of oligæmia. The more extreme varieties of acute anæmia are always attended by breathlessness more or less considerable in degree, which manifests itself objectively by increased depth and frequency of the respiratory movements, subjectively by a peculiar craving for more air. We cannot be far wrong in attributing the urgent dyspnœa which invariably attends severe bleeding—and which, as has already been pointed out, may even culminate in an outbreak of general convulsions—to the sudden arrest of the supply of oxygen to the respiratory centres, the immediate stimulus being furnished either by the want of oxygen, or, more probably, by the accumulation of poisonous intermediate products of tissue metamorphosis in the blood. In the subacute and chronic forms of anæmia, on the other hand, the dyspnœa takes the form of a habitual, though moderate increase in the number of respirations per minute, without any increase in the depth of each individual respiratory act. The patient is unconscious of its existence, save when he undertakes any violent exertion or suffers from emotional excite-

ment. Under these circumstances, the dyspnœa may suddenly become exaggerated into a feeling of positive anguish, with tumultuous, panting respiration. The constant though inconsiderable quickening of the respiratory movements in anæmic persons is due to a complex variety of causes. It does not at present admit of being perfectly explained. It is probably due, in the first place, to an increased excitability of the respiratory centres, which take part in the irritable weakness common to the whole of the nervous system; secondly, to the imperfect decarbonization of blood in the lungs, owing to lack of oxygen, the pulmonary fibres of the vagi being stimulated and quickening the respiratory movements. For since the exhalation of carbonic acid is intimately connected with the absorption of oxygen by the blood (Ludwig and others), and since carbonic acid is known to stimulate the pulmonary terminations of the vagi (L. Traube), we may infer, first, that oligocythæmic blood is not only poorer in oxygen, but contains more carbonic acid than normal blood (Thiry); secondly, that it increases the frequency of the respiratory movements through the accelerating fibres of the respiratory nerves. Further, violent dyspnœa, both objective and subjective, must inevitably set in whenever the proportion of carbonic acid in the blood is rapidly augmented; for we know that any considerable excess of carbonic acid in the blood is equivalent to acute privation of oxygen in stimulating the respiratory centre and giving rise to intense breathlessness (L. Traube, Dohmen, Pflueger, Nasse, and others). But an excess of carbonic acid is retained in the blood whenever the pulmonary circulation stagnates, and the distribution of the blood becomes irregular, owing to momentary fatigue of the heart. This is why anæmic persons speedily become breathless during their painful attacks of palpitation, and why the dyspnœa usually lasts for some time after the attack is over. Its severity does not abate until the exhalation of the retained carbonic acid has been completed by a suitable re-establishment of the pulmonary circulation. The breathing then returns gradually to its habitual type—moderate acceleration of rhythm, with shallowness of the respiratory movements. Lastly, it is plain that the exceptionally severe dyspnœa brought on by violent exertion is due not merely to the fatigue of the heart and consequent retention of carbonic acid in the blood, but, in at least an equal measure, to the increased formation of carbonic acid which results from muscular contraction.

5. *Remaining organs of the body.*—The functional disturbances manifested by the other organs of the body in anæmia may be dismissed in a few words, for they originate, for the most part, in conditions that have already been discussed. My remarks will therefore be confined to those points which have an immediate bearing on the matter in hand, and which have not been elucidated, or have been insufficiently elucidated, on former occasions.

Anæmic patients often suffer from functional disorders of the digestive apparatus, which generally belong (when really consequences and not causes of the anæmia) to the "atonic" variety of dyspepsia, whose mode of origin and essential character, as well as its relation to oligæmia, have already been analyzed (pp. 334 and 374).

A peculiar, also functional disturbance of the digestive system is the anorexia which is almost always present in the more severe forms of acute anæmia. Its mode of origin is still obscure. On the other hand, the paroxysmal craving for food by which many anæmic patients, especially those recovering from acute disease, are tormented, and the feeling of satiety that treads closely upon its heels, may both be traced to the irritable weakness of the nervous system, and belong to the category of morbidly exaggerated common sensations. Finally, the thirst which comes on after great loss of blood is due to the absorption of large quantities of liquid from the tissues into the vascular system. It results immediately from the dryness of the tissues, and also occurs from similar causes in febrile anæmia. The mucous lining of the mouth and fauces shares in the general dryness of the tissues; hence, the afferent nerves are subjected to that specific form of irritation which gives rise to the feeling of thirst under normal conditions.

The integument presents highly important and characteristic changes, both in its vascularity and in its nutrition. Concerning its functional state, not much of a positive kind can be affirmed.

One is certainly tempted to ascribe the defective secretion of sebaceous matter, and the diminished perspiration *occasionally* observed in anæmic persons, to the changes that have taken place in the nutrition of the skin—changes in which the cutaneous glands not unfrequently take part by undergoing atrophy and degeneration. And, so far as the sebaceous secretion is concerned, this view would not be inappropriate; for it does, for the most part, diminish as the marasmus increases. On the other hand, the behavior of the sudoral secretion in anæmic persons is very capricious. For instance, it would not be difficult to show that the activity of the sudoriparous glands is occasionally—even when the anæmia is extreme and the marasmus most advanced—not only not lessened, but actually and enormously increased. I need only mention the colliquative sweating of phthisis, the profuse sweating that occurs in the collapse of acute anæmia, the hyperidrosis of the dying. The two last-named examples prove that the quantity of blood in the skin has no more to do with the amount of perspiration than extreme general anæmia or the most advanced marasmus. The hyperidrosis observed during collapse or just before death coincides with a pale, cold, bloodless skin; on the other hand, even active hyperæmia of the skin is not necessarily attended by sweating. No causal connection can, therefore, be established between the quantitative modification of the perspiratory function in anæmia, and the altered distribution of the blood, or variations of blood-pressure, of vascular tonus, etc. It is more correct to ascribe all changes in this secretion to the paramount influence of the nervous system; when anæmic persons perspire copiously, the phenomenon must be viewed as accidental, rather than as being of the essence of the anæmia. Accordingly, it does not, strictly speaking, fall within the limits of our subject. Still, there is one sense in which hyperidrosis may possibly be regarded as an effect of anæmia. The latter condition may give rise to disturbances of innervation of a kind invariably productive —whatever may have been their origin—of increased sudoral secretion. Concerning the nature of these disturbances we may, indeed, be allowed to speculate; but of positive information we have none to give.

Section of the cervical sympathetic is known to be followed by unilateral sweating of the face and upper part of the body. Section of the *medulla oblongata* in the horse (life being kept up by artificial respiration) gives rise to profuse sweating all over the body. These facts make it probable that the sudoral secretion is regulated by the brain, or, in other words, that the nerve-centres exert an inhibitory influence on the sudoriparous glands, the withdrawal of which influence is followed by hyperidrosis. The unilateral sweating after division of the sympathetic is commonly regarded as a vaso-motor phenomenon, and connected with the vascular relaxation which is the characteristic effect of that lesion. This view would seem reasonable enough, were it not that hyperidrosis, as I have already pointed out, may also occur under an exactly opposite set of conditions, viz., when the skin is remarkably bloodless. Hence, it is certainly more logical to view the cutaneous hyperæmia and the hyperidrosis as co-ordinate effects, instead of assuming the former to be the cause of the latter. But if we give up the notion that the sweating results from division of vaso-motor fibres running from the brain to the integument, we must ascribe it to division of inhibitory fibres. This hypothesis at once explains why commencing cerebral paralysis (during a state of collapse, before death, before a fainting-fit) should be so often associated with profuse sweating, notwithstanding the bloodless condition of the skin.

The urinary secretion does not obey the same laws as the perspiration, its quantity being more immediately dependent on mechanical conditions, and more liable, therefore, to be influenced by changes in the pressure and the composition of the blood. The greater the volume of the blood, the more dilute it is, the more vigorous the heart's action, the more rapidly will a watery secretion filter through the Malpighian tufts into the efferent canals of the kidney. This explains why the secretion of urine, just after severe hemorrhage, is almost always very scanty, speedily returning to its normal amount as the total volume of the blood is restored by absorption of water, and the heart regains its power. As the subacute and chronic forms of anæmia are usually associated with hypalbuminosis, and the latter facilitates the process of filtration through the kidneys, the flow of urine is not generally much reduced, save when there happens to be profuse sweating, or when (as in fever) the insensible exhalation from the lungs and skin is much increased. The facts concerning the quantitative alterations in the amount of urea and urinary pigment excreted by anæmic persons have already been stated in the section on General Symptomatology. I need only add that although the elimination of uric acid in anæmic subjects does not stand in any constant relation to the state of the blood, it nevertheless appears, like that of urea, to fall below the normal standard.

The state of the sexual functions still remains to be considered. First, as regards the male. Whereas, in many cases of anæmia, the sexual function is simply torpid (lessened or extinct), in others—in the majority—it presents the characters of irritable weakness (the sexual appetite is easily awakened, seminal emissions are frequent, erection is frequent though incomplete, premature ejaculation occurs during coitus, etc.). There cannot be a doubt that these phenomena are simply localized manifestations of the general change affecting the nervous system in anæmia, and that they are closely analogous to the corresponding symptoms exhibited, *e. g.*, by the heart. It may be affirmed, broadly, that the irritable weakness of the male generative organs, like that of the heart, is chiefly associated with the milder forms of anæmia; while the more extreme forms of anæmia and marasmus are more usually attended by complete extinction of the generative function, analogous to the "permanent feebleness" of the heart. I do not mean to deny the exceptions to this rule, for it is undoubtedly true that every particular province of the nervous system possesses a certain measure of individual autonomy which is especially prone to assert itself under pathological conditions. Lastly, I may as well state that the term "irritable weakness," which I have repeatedly employed in a general sense to denote a definite morbid condition of the nervous system as a whole, is commonly used in a more special sense to express the corresponding disorder of the male generative functions. It is in this latter sense that the term is generally understood, when not guarded by some explanatory prefix.

In anæmic females the generative function does not present any constant alteration. It sometimes plays an important part in aggravating the anæmia (p. 324). The very variable behavior of the menstrual discharge is of great interest from this point of view; in many cases of anæmia it grows scanty, or ceases to flow altogether; in others again it continues unimpaired, and helps to exhaust the patient's strength. Now, although it is not surprising that the menstrual function should be interfered with, or even suppressed in general anæmia and advanced marasmus, the opposite phenomenon cannot but excite our wonder and elude our attempts at explanation. Still, if we bear in mind that the menstrual hyperæmia of the generative organs, looked at from the physiological point of view, is not so much the cause as the consequence of the periodic maturation of ova, the continued occurrence of the menstrual flow in many cases of general anæmia will only indicate that the process of ovulation persists in its normal course, and continues to provoke that vehement afflux of blood to the genital organs which culminates in the monthly discharge. Inasmuch, moreover, as the periodic maturation of ova is a result rather of an inherent stimulus than of any impulse communicated to the ovary from without, we can see why the process in question should go on for a considerable time, even when the organism, as a whole, is badly nourished, before it succumbs to adverse circumstances. We can also understand, further, that the menstrual flow may continue abundant, or even excessive, notwithstanding the presence of anæmia, so long as the hyperæmiating stimulus propagated from the ripening ovule to the entire genital apparatus is strong enough to attract a considerable portion of the whole blood to the sexual organs, and, indirectly, to cause rupture of the distended blood-vessels of the uterine mucous membrane. Lastly, we are enabled to see why so many anæmic women continue not only to menstruate profusely and regularly, but to conceive and to bear children. For these ulterior developments of the sexual function require nothing more than the intervention of the male element in due time and place. I have already alluded to the fact that anæmic girls and women are very prone to suffer from leucorrhœa (p. 354), and that this affection should be viewed as a true symptom of anæmia, since it may be cured by constitutional measures directed against the anæmic state without special local treatment. We are not at present in a position to account for the causal relation between the two sets of phenomena. Moreover, the chronic catarrh of the genital mucous membrane on which the leucorrhœa depends may be quite as legitimately included among the complications and sequelæ as among the sexual symptoms of anæmia.

Complications and Sequelæ.

As most forms of well-marked anæmia are symptomatic and proceed from other pre-existing maladies, it is clear that the symptoms of the consecutive anæmia will often combine with those of the primary disease to form a complex whole. I need not here recapitulate the manifold variety of such complications, or consider all the possible modifications that may be introduced into the proper symptoms of anæmia by those of the primary affection. These are not, strictly speaking, complications of anæmia; on the contrary, the anæmia may be said to be a sequela, or a complication of the morbid process to which it owes its origin, and with whose continuance its own is often most intimately bound up.

On the other hand, we have a perfect right to speak of genuine complications of anæmia whenever an anæmic patient is attacked by any sort of new disease, independent of, though coinciding with the anæmia. This conjunction is at least as common as the opposite one of which I have spoken above. Anæmic persons are, upon the whole, more liable to disease than those who are in health. They are, roughly speaking, more prone to suffer from other maladies, whether constitutional or local; nay, the susceptibility to certain morbid processes is so greatly increased by the presence of anæmia that they may fairly be brought into genetic connection with it. When we find it stated, on the one hand, that an exactly opposite relation holds good for many diseases—more especially certain acute febrile processes which are said to attack healthy persons more often than those who are anæmic (*e. g.*, enteric fever, acute rheumatism, pleurisy), we must recollect that healthy people are much more exposed to particular injurious influences, owing to their occupation, their more irregular life, etc., than anæmic invalids; further, that the latter are quite as liable, sometimes more liable to be attacked than the former, when placed under similar conditions. Statistical records of the frequency of particular diseases used formerly to be quoted as evidence of the comparative immunity of anæmic persons from, *e. g.*, lobar pneumonia; more recently, however, they have pointed to an entirely opposite conclusion, so that the doctrine of the relative insusceptibility of the anæmic to acute disease has been falling more and more into discredit.[1]

The increased susceptibility of anæmic persons to disease appears to be intimately associated with their defective nutrition; the tissues are less able to resist injurious influences, the organism to regain its equilibrium after momentary disturbance. Not only, therefore, are the tissues of the anæmic more liable to disease, but they show less disposition to spontaneous repair. Indeed, the affected part usually exhibits a decided tendency to undergo destructive change—necrobiosis—easily explained by the defective supply and faulty composition of the nutrient fluid. There is yet another way in which the presence of anæmia helps to modify the character of many trivial disorders in an unfavorable sense: any active excitement of the nervous system is usually followed by premature functional exhaustion when the symptoms of cardiac feebleness start at once into a threatening prominence.

I must now enumerate the more important diseases whose exceptional prevalence among anæmic persons renders it likely that they stand in some intimate relation to the anæmic state. Among affections of the respiratory apparatus, pulmonary phthisis deserves the first place as a frequent sequela of anæmia, whether the latter be of idiopathic or of symptomatic origin. It has long been recognized that, notwithstanding an inherited predisposition to phthisis, the actual outbreak of the disease may often be delayed for a long time—perhaps altogether prevented—by a careful tonic regimen; whereas it is very likely to insinuate itself into the system, when anæmia has unfortunately been allowed to establish itself. Thus, for example, severe febrile disorders, especially enteric fever, often leave a tendency to phthisis, together with a lingering anæmia, behind them; and when once the pulmonary mischief has broken out, it usually runs an exceptionally rapid and destructive course. But pulmonary consumption is quite as liable to break out in cases of symptomatic anæmia due to exhausting discharges. The number of nursing mothers affected by it illustrate this statement. So, too, want of the necessaries of life, over-fatigue, depressing emotions—in a word, all the causes of idiopathic anæmia referred to above, are capable of exciting phthisis, the anæmia furnishing the soil in which the pulmonary disease springs up. I need not enter more deeply into the nature of the connection between anæmia and phthisis. The reader will find what information he requires in the chapter on the etiology of the latter disease.

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[1] An obvious exception to the general rule that anæmic persons are specially liable to become affected by other diseases, is furnished by such maladies as gout, the oxalic acid diathesis, and others, which stand in an unmistakable relation to a "plethoric" habit of body. (Cf. p. 308.)

Among affections of the digestive apparatus, gastric ulcer is remarkably common in anæmic subjects. This point is worthy of special notice, as gastric ulcer may easily be confounded with the nervous cardialgia which is also not uncommon in the anæmic. Accordingly, when we find an anæmic person troubled with serious gastric symptoms, we must always bear in mind the possibility that an ulcer may be present, and the routine treatment of the constitutional disorder must be modified accordingly. Gastric ulcer may exist without betraying its presence by paroxysmal cardialgia; it may remain latent till an attack of profuse hæmatemesis or of fatal peritonitis from perforation brings it suddenly to light. Such melancholy accidents may occur from an ulcer which has become insidiously developed during an attack of anæmia, and are then usually quite unexpected. The frequent occurrence of perforating ulcer in anæmic subjects is probably connected in some way with their liability to disease of vessels (particularly fatty degeneration of the arterial intima and of the capillary walls). For information about the intimate nature of this connection, the reader is referred to the chapter on Gastric Ulcer.

Among structural diseases of the nervous system I must allude to cerebral hemorrhage, which is occasionally met with in anæmic patients. It gives rise to the clinical symptoms of apoplexy, and generally ends in death. It may be attributed, like gastric ulcer, to previous changes in the vascular walls. Though it is fortunately uncommon in anæmia, it is especially striking when it does occur, for the victim is generally young, at an age when sanguineous apoplexy is among the rarest of events.

A brief record of two cases that occurred in my own practice will serve to illustrate the above remarks.

1. Lad of sixteen, convalescent from enteric fever; his temperature has been normal for about four weeks. Sudden symptoms of apoplexy without definite hemiplegia. Death in a few hours, with tracheal râles. On post-mortem examination, abundant hemorrhage into left lobe of cerebellum, whose tissues are extensively broken up; an effusion of blood along the entire base of the skull.

2. Girl of eighteen, convalescent from enteric fever two months; still pale and weak. Sudden apoplexy, with left hemiplegia. Death. Large clot in right *corpus striatum*, with effusion of blood into the lateral ventricles.

Functional disorders of the nervous system are extremely common in anæmic subjects, and form a majority of all the complications of anæmia. They must be viewed broadly as exaggerations, *i. e.*, as outgrowths of the general state of nervous irritability which have assumed a certain independence. Hence, it is not easy to draw the line between those neuroses which are true complications and those which are merely symptoms of anæmia. The distinction between the two must always be to some extent arbitrary. In the female, and more rarely in the male sex, the general hyperæsthesia, the increased reflex excitability, the capricious psychical condition, occasionally become exaggerated into well-marked hysteria, whose symptoms may be so pronounced as to throw the remaining phenomena of the anæmic state more and more completely into the background. Since it is not always in the more intense forms of anæmia that hysteria is developed, we may conclude that a decided tendency to hysterical disturbance of the nervous system precedes the anæmia, the latter serving only to provoke an outbreak. In other cases, however, the genetic relation between the anæmia and the hysteria is more distinct and exclusive. There is no history of any previous tendency to nervous disturbance. Symptoms of decided hysteria make their appearance suddenly after debilitating influences of one kind or another have brought on well-marked anæmia. These symptoms subside as the anæmia disappears. Whether the anæmia be the essential or only an auxiliary cause of the hysteria, the duration of the latter depends in some degree on that of the former. We can never reckon on the disappearance of the hysteria while the anæmia lasts. Hence, as the two maladies often exist together, we ought never to limit our attention, in a case of hysteria, to the female generative organs; we ought always to be on the lookout for signs of anæmia, and if we discover any such, to combine general tonic measures with our local applications to the catarrhal erosions of the *portio vaginalis*, etc. Though it would be a mistake to suppose that anæmia lies at the root of every case of hysteria, still, the number of cases in which we may legitimately infer that the two affections are more or less connected with each other—either from the behavior of the organism as a whole, or from the effect of our remedies—is relatively considerable. Other neuroses, *e. g.*, chorea, are prone to occur in anæmic persons, and stand in much the same relation to the blood-change as hysteria. Lastly, a number of psychoses, some characterized by depression, others—a majority—by excitement, seem frequently to occur in causal connection with anæmia, for treatment directed against the latter is occasionally followed by improvement or even cure of the former. But our insight into the nature of the connection of these and other neuroses with anæmia is still very imperfect; further speculation on the subject would therefore be at present premature.

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Diagnosis.

There is no difficulty in recognizing anæmia from loss of blood when the bleeding takes place externally, either in our presence, or leaving manifest traces behind it (wounds, clots, etc.); but when, as in internal hemorrhage, there is no visible evidence to be had, we are justified in regarding it as the cause of an acute anæmia when we find sudden and intense pallor of the skin and mucous membranes associated with an extremely small pulse, faintness, and a tendency to actual syncope on assuming the erect posture. Similar signs of collapse may, indeed, be produced by cardiac weakness from other causes; but we may nearly always obtain a clue to the right interpretation of the phenomena by considering all the circumstances of the case. If the patient happen to have been suffering from some disease attended by a liability to internal bleeding—if the collapse was preceded by symptoms indicative of rupture of a blood-vessel, with extravasation into one of the great cavities of the body (*e. g.*, sudden and acute pain)—if, lastly, we are able to demonstrate progressive dullness on percussion in the dependent parts of the thorax or abdomen, we may consider ourselves entitled to diagnose "acute oligæmia from internal hemorrhage." Bearing the above remarks in mind, we shall not fail to recognize the rupture of an aneurism, or of the sac in tubal gestation, even during life. Should the above symptoms be absent, however, the case may remain obscure till cleared up by post-mortem examination, *i. e.*, we shall not be able to decide whether it is one of acute anæmia from inward bleeding, or of fatal collapse, with paralysis of the heart, from some other cause.

The diagnosis of chronic anæmia depends quite as much on a due estimate of any primary disease from which the patient may be suffering, and of his mode of life, as upon his outward aspect and the impairment of his bodily energies. We may reasonably suspect the existence of chronic oligæmia whenever we are able to recognize conditions hostile to sanguification, or likely to hasten the consumption of the blood (cf. Etiology); our suspicions being confirmed by the patient's pallid complexion, the marasmus, the sluggish feebleness of all the vital processes—especially voluntary movement. Thus the presence of chronic anæmia is usually recognized without much trouble; and its recognition is usually attended by a discovery of its causes. I mean that we are able, not merely to affirm that the anæmia exists, but to prefix some special epithet indicative of its origin.

Duration, Issues, Prognosis.

The duration of anæmia is extremely variable. It varies within the widest possible limits, from the acute anæmia due to hemorrhage which ends fatally in a few minutes, to those extremely chronic forms of the malady which linger on for years—nay, for a lifetime.

The following remarks are meant to illustrate the connection between the duration of anæmia and the causes to which it owes its origin.

When death is immediately due to loss of blood, it may roughly be said to occur earlier in proportion as the blood is poured out more quickly. Hence, it is most sudden when the hemorrhage is due to wounding of large arteries, to rupture of an aneurism, to extensive cuts. Should the patient survive, the time spent in convalescence will depend, first, on the amount of blood lost; secondly, on conditions, external and internal, peculiar to the individual. Foremost among these are age and constitution; advanced age and a relaxed habit of body retarding, youth and vigor hastening recovery. The influence of sex is less decided; there is reason to believe, however, that although the immediate risk from hemorrhage is greater for the male than for the female (cf. p. 297, and the subsequent remarks concerning prognosis), the former is, upon the whole, better able than the latter to make good the loss sustained. At any rate we are more accustomed to see profuse bleeding followed by imperfect recovery—by permanent anæmia of a moderate kind—in women than in men. Lastly, as regards outward conditions. The care taken of the patient, the adoption or neglect of strengthening measures, have much to do with the time he takes in getting well; so that we cannot exactly—*i. e.*, in days or weeks—predict the total duration of the malady or that of convalescence. I need hardly say that the notion that a loss of blood amounting to one-sixth of its entire volume requires a period of six weeks to make it good is wholly arbitrary and unsustained by facts.[1]

Still less are we able to foretell the probable duration of anæmia in its remaining forms. The time required for the evolution of the disease depends, primarily, upon the persistence or disappearance of its cause. It may be stated, generally, that we can only reckon on a term being set to the malady when it is due to a removable cause. Should the cause not be capable of removal, the consecutive oligæmia will likewise persist, its manifestations being only held in check by a continuous employment of therapeutic and dietetic measures. Thus, for example, a certain degree of anæmia is always present in chronic albuminuria: it may be kept down, though not eradicated, by a suitable supply of nourishment. But there are many causes of anæmia which are not only incapable of being removed, but whose consequences cannot even be checked by appropriate treatment; the anæmia assuming a progressive and malignant character, and usually terminating in death. Thus persons suffering from phthisis, cancer, etc., ultimately succumb to anæmia and marasmus, though the duration of life may vary widely in different cases.

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[1] Another instance of this cabalistic use of numbers is the doctrine that the probable crisis of certain diseases (*e. g.*, lobar pneumonia) must occur on one of the odd days, counting from the day of invasion!

But if the cause of the anæmia be a removable one, or if it disappear after a time of its own accord, the further duration of the disease will depend partly on its own intensity, partly on the conditions, external and internal, to which the patient is exposed (*vide supra*). Accordingly, the time taken up in convalescence varies still more considerably in these cases than in acute anæmia.

Anæmia may end in death or in recovery, and the latter may be complete or incomplete.

In acute anæmia after hemorrhage, death results from an arrest of the supply of oxygen to the respiratory centres in the brain—it is of cerebral origin. I have already explained (p. 389) that privation of oxygen, when sudden and severe, stimulates the ganglia at the base of the brain very powerfully in the first instance. Hence, the fatal issue which immediately succeeds the phenomena of irritation (dyspnœa, general convulsions) may fairly be ascribed to progressive exhaustion and ultimate paralysis of those motor centres—exhaustion and paralysis consequent on over-stimulation. On the other hand, when the lack of oxygen makes itself felt slowly and gradually, the signs of violent excitement do not show themselves, and death results from an immediate depression and ultimate annihilation of the excitability of the *medulla oblongata*. The probable reason of this difference between the effects of sudden and those of gradual privation of oxygen has already been discussed. When death does not occur immediately after great loss of blood, but is delayed until the patient has rallied, or strikes him unexpectedly when well on his way towards recovery, it is almost invariably due to syncope. Now, although in this, as in the foregoing instance, cessation of the respiratory movements and of life are *immediately* due to extinction of the irritability of the respiratory centre, still the two must not be confounded; in the case we are now considering, the primary change—antecedent to paralysis of the medulla—is the disturbance in the circulation through it, caused by paralysis of the heart; the mode of death is "cardiac" as contrasted with "cerebral." This view is confirmed by the fact that the fatal issue is usually brought on by accidents—such as muscular effort, emotional excitement, etc.—tending to lower the action of the heart.

In the remaining forms of anæmia the patient may likewise succumb to cardiac paralysis in the accidental manner just described, the paralysis being due to temporary over-exertion of the heart. But, in the majority of cases, the anatomical starting-point of the fatal symptoms cannot be precisely determined; all the vital functions being ultimately extinguished together—becoming exhausted—in consequence of the general state of marasmus.

Acute oligæmia from loss of blood usually terminates in complete recovery when the bleeding has not been excessive and has been checked in time, either by nature or by art. Although a patient who has lost a good deal of blood may continue liable for a long time (days and weeks) to be carried off by unforeseen syncope, still, if appropriate measures have been taken and his constitution be a healthy one, the cessation of the hemorrhage is usually a guarantee for the preservation of life and the possibility of complete recovery. Whether this possibility be subsequently realized, or whether, for reasons to be alluded to hereafter, the patient's restoration be incomplete, the renewal of the blood invariably proceeds in a certain definite order. First, a quantity of water is taken up from the tissues and the alimentary canal; next, the crystalloid and colloid elements of the plasma; and finally, the red corpuscles, are completely or partially restored.

Although the precise origin of the red corpuscles is still obscure, there can hardly be a doubt that they are developed, by gradual metamorphosis, from the colorless corpuscles in the spleen, the lymphatic glands, and the marrow of the bones. During the first few days after a profuse hemorrhage (p. 327) a vast number of leucocytes immigrate into the blood from the cytogenic organs, the process of immigration going on for some time, though at a slower rate. A certain proportion of the immigrant elements (the uninuclear, not the multinuclear ones, Virchow) appear to undergo metamorphosis. Some observers (Koelliker, Erb, Golubew) describe the process as a gradual reddening of the corpuscular protoplasm, followed by disappearance of the nucleus and a simultaneous development of the central concavity characteristic of the newly-formed disks. Further investigation is required before these statements can be adopted as final.

Of course we have no certain means of judging if the restoration of the blood after hemorrhage be really complete. From a clinical point of view, however, we may legitimately affirm recovery to be complete when, after the lapse of some weeks or months, the patient's aspect and functional energies leave nothing to be desired.

In other forms of anæmia complete recovery is possible only when the causes of the malady admit of being rooted out. But even when they do, the chances of recovery being complete are no greater than they are after loss of blood from hemorrhage. As a general rule, perfect restoration to health can only be anticipated when the blood-change has not been too profound, when the patient is suitably taken care of, and when his powers of repair are really adequate to bring back the composition of the blood to its original standard.

In a very large proportion of cases, finally, recovery is incomplete. Apart from complications and sequelæ, which may hinder the reparative process and give rise to further troubles, the continued operation of the original causes of the anæmia too often bars the way. Even when these causes are effectually neutralized, either spontaneously or by the help of art, complete recovery may be prevented by the absence of the necessary food, rest, etc. Again, there may be some internal condition, peculiar to the individual, which tends to perpetuate the anæmia, *e. g.*, when the latter has reached a degree of intensity beyond that which the recuperative powers of the organism are adequate to meet. Under such circumstances the defective state of the blood is indeed remedied—but never perfectly. The patient is left in permanent ill-health, which, owing to the absence of any ascertained local disease, can only be attributed to the continued presence of anæmia.

This state of things is often observed in women who have rallied from profuse post-partum hemorrhage. Old people, again, and persons of relaxed habit, after undergoing some exhausting illness from which they barely escape with life, not unfrequently stop short of complete restoration to health—in common parlance, "they never are themselves again." This means, in other words, that a certain measure of anæmia and marasmus is left and obstinately resists all our attempts at cure.

This singular result admits of only one explanation. The organism, once affected by severe anæmia, possesses only a limited power of regenerating those blood constituents which it has lost, even under favorable conditions of diet, rest, etc. The capacity of the digestive apparatus for assimilating nutriment and the productive activity of the cytogenic organs are restricted within definite limits, which are further narrowed by the existing anæmia itself. The anæmic patient labors with enfeebled powers at the heavy task of his physical regeneration. All the while he is obliged to meet the demands of his daily expenditure; and just as many a man, however frugal he may be, fails to climb out of the abyss of bankruptcy into which he has once fallen, so the task of the anæmic patient may be altogether beyond his powers, and he may be condemned to see it remain imperfectly fulfilled. Lastly, it is self-evident that the difficulty of the task will stand in an inverse ratio to the recuperative powers with which the individual is endowed. Old people will be at a greater disadvantage than those in the prime of life or than children—persons of torpid habit than those with a tough constitution (p. 306)—women (upon the whole) than men, etc.

The prognosis in anæmia depends, primarily, on the intensity of its cause. This is true of acute anæmia, in which the clue to a prognosis is furnished by the ratio between the amount of blood lost and the total volume of that fluid. It is also true of the various forms of oligæmia; the abundance of a discharge, the severity of a digestive disorder, the intensity and duration of a fever, etc., indicating the degree of danger in any particular case.

As regards the prognosis in acute anaemia after hemorrhage, the following empirical law may be regarded as approximately correct. A single bleeding, which amounts to one-half of the total volume of blood in the body (in adults from 2.5 to 3 kilogrammes—from five to six pints), is almost certain to prove fatal. When the same proportion of the blood is lost by recurrent hemorrhages, the prognosis is, of course, more hopeful; on the other hand, circumstances peculiar to the individual may render a comparatively slight loss productive of serious consequences. I refer more especially to the influence of age; infants are in extreme danger when they have lost fifty grammes (one and three-quarter fluidounces), children during the first years of life, when they have lost two hundred grammes (eight fluidounces) of blood. So too, old people, those who are already exhausted by disease, corpulent and torpid persons, bear even small losses of blood very ill, and succumb to hemorrhage with astonishing facility. Next, as regards sex, men bear great and sudden loss of blood worse than women. These individual differences, so important in relation to prognosis, have been partially accounted for already in the section on Etiology. I need only repeat that the relatively small amount of blood possessed by young children, together with the rapidity of their growth, and their consequent need of nutrient matter, are probably at the bottom of their susceptibility in this matter. The slow renewal of the blood in old people, and those who are exhausted by disease, must necessarily reduce their power of resistance to a disproportionate extent. Lastly, as regards the inferior tolerance of males for sudden and profuse hemorrhage, this peculiarity may be connected with the greater energy of their nutritive processes, in consequence of which the body is continually making greater demands upon the blood for pabulum and oxygen. Further, I ought to add that the remarkable power of females to bear great loss of blood is chiefly manifested during parturition, and is much less decided on other occasions, *e. g.*, when bleeding takes place from the bowel in enteric fever. There is undoubtedly some special reason for the fact that women are able to lose an astonishing quantity of blood during delivery without danger to life. The phenomenon may possibly be accounted for by reflecting that, in the act of parturition, a parasitic organism (*sit venia verbo*), which has hitherto drawn its nourishment from the female body, is got rid of; the loss of blood may thus be regarded as tending in some measure to ward off a risk of plethora.

Next in importance to the quantity of blood lost—as regards danger to life—is the rate at which it is poured out. Arterial bleeding, both on account of its rapidity, and because arterial blood is highly oxygenated, is peculiarly dangerous, especially if it occur from one of the larger arteries. The *medulla oblongata* is quickly deprived of oxygen; hence, speedy exhaustion of the respiratory centre. When the bleeding is gradual, a better prognosis may be given; not only is there more opportunity for therapeutic intervention, but the physiological renewal of the wasted blood is more successfully effected.

Lastly, the situation in which bleeding occurs may be as important as its abundance and rapidity. I need hardly point out that internal hemorrhage is usually, *cæteris paribus*, far more dangerous than that which takes place within reach of hæmostatic measures. The rapidity and care with which such measures are carried out is of the first importance as regards prognosis in any particular case; for the danger increases in proportion as the bleeding is left to itself.

In other forms of anæmia likewise, whether subacute or chronic, the patient's prospects are largely influenced by the possibility of effecting a speedy removal of the efficient cause of the disease. (I have already alluded to the intensity of the cause, and the length of time it has been in operation, as essential elements in arriving at a prognosis.) Those prospects are least hopeful when the cause of the anæmia is, or appears to be, ineradicable, and when the disease itself is severe and progressive. These characters are met with in combination, *e. g.*, in many cases of anæmia due to hectic fever and to the cancerous cachexia. In these, the prognosis is of course a gloomy one, not merely as regards recovery, but as regards life itself. Though far from good, it is somewhat better when, though the cause of the anæmia does not admit of removal, the blood-change itself is not far advanced, and is maintained *in statu quo* by suitable dietetic and other measures. Here, of course, perfect recovery is out of the question. A permanent though moderate albuminuria, residual from previous kidney-disease, is often associated with a corresponding degree of consecutive anæmia; but with suitable precautions as regards diet and regimen, the latter may last for years without any appreciable detriment to the patient.

Finally, the prognosis is most favorable when the cause of the oligæmia admits of being speedily and completely removed, or when it disappears of its own accord at an early period. Should the anæmia not be too severe, should the patient be situated under favorable circumstances, external and internal (mode of life, age, constitution, etc.), we may anticipate his complete recovery with much confidence. I need hardly explain why, on the other hand, intensity of anæmia, unfavorable environment, insufficient recuperative power, should modify our prognosis for the worse, even when the primary causes of the malady have been got rid of, and the *indicatio morbi* alone remains to be fulfilled.

Treatment.

Prophylaxis.

The prophylaxis of anæmia is one of the most important problems of hygiene, both public and private; indeed, it is all but coextensive with the latter. On the one hand, the idiopathic forms of anæmia originate, for the most part, in some quantitative or qualitative defect in the requirements essential to life—in some deficiency or one-sided excess of the necessary vital stimuli. On the other hand, the main business of practical hygiene is to harmonize and regulate those outward conditions, whether for the individual or for the community. Hence, it is clear that the development of anæmia will be prevented in proportion as the purposes of hygiene are carried out successfully. Again, since a great variety of morbid processes contain within them the germs of symptomatic anæmia, the fulfilment of that other task of hygiene, viz., the annihilation of the causes of disease, must indirectly contribute to prevent the malady with which we are at present concerned. Lastly, all those strictly remedial measures designed to render severe diseases (*i. e.*, such as give rise to anæmia) abortive, or to prevent the inanition and consumption of the blood which are normally associated with them, belong likewise to the prophylaxis of anæmia.

The subject, as I have just sketched it, is obviously too vast to be fully considered in this place. We shall have to compress its most important parts, as it were, into a nutshell, since volumes might easily be filled by discussing them in detail.

For the prevention of anæmia in the healthy subject, the first requisite is a dietary capable of supplying those constituents of the blood which are consumed during the organic processes. Foremost in importance is an adequate supply of albuminates, of the truly plastic food-stuffs, any lack of these being immediately followed by hypalbuminosis and marasmus. The non-azotized food-stuffs (fats, amyloids, sugar) and the nitrogenous gelatin-yielding compounds are likewise very important, partly as sources of energy, partly for the conservation of the albumen of the blood and tissues (p. 311). Hence, a liberal admixture of these substances with the albuminates contributes very essentially to maintain the balance of nutrition. Apart, then, from the pecuniary reasons which make a pure meat diet (or, to speak more generally, an albuminous diet) difficult, and for large classes of the population wholly impossible, a mixed diet is certainly the most suitable one for man as an omnivorous animal.

Whether as regards the absolute amount of food required, or the relative proportions of its several constituents, the opinions of various authors (Liebig, Moleschott, Playfair, Voit, etc.) differ not inconsiderably from one another. From the data at our disposal, however, we may confidently affirm that the adult male requires from about 500 to 700 grammes (from sixteen to twenty-two ounces) of food daily, on an average; one-fifth or one-sixth of this quantity consisting of plastic material (albumen). To this must be added a large supply of water (2,500 to 3,000 grammes a day). Adding the liquid to the solids, we find the total ingesta of the adult male amounting to from 3,000 to 3,500 grammes *per diem*, or, in other words, to about one-twentieth or one-twenty-fifth part of his body-weight (40 to 50 grammes per kilogramme).

J. von Liebig ascertained that the daily rations issued to the Hessian troops amount to 75.74 grm. of albumen and 447.86 grm. of non-azotized matter; total, 523.6 grm. of solid food; the ratio of albumen to non-nitrogenous compounds being, on this calculation, about 1 to 6. Playfair reckons the average daily ration of English convicts at 490 grm. (60 grm. of albuminates, 430 grm. of carbo-hydrates and fats). In this very restricted dietary the proportion of albumen does not amount to one-seventh of the other constituents. Voit gives 560 grm. as the average daily ration of the Bavarian private (exclusive of inorganic constituents). This total includes 133 grm. albumen, 427 grm. fats and carbo-hydrates. Besides being absolutely more liberal, this dietary contains a much larger relative proportion of albumen, the ratio of nitrogenous to non-nitrogenous constituents being as 1 to 3.2. Moleschott's inquiry into the average ration issued in the Italian army gives the following results: albuminates, 125 grm.; fats, 25.1 grm.; carbo-hydrates, 470.9 grm.; in addition to these, 24 grm. of alcohol, and 27.6 grm. of inorganic solids. The ratio of albuminates to carbo-hydrates and fats amounts to 1 : 3.96, or nearly 1 : 4. The latter figures tally very closely with the statements previously made by the same author[1] concerning the average total and proportionate composition of the daily ration of an adult laborer—statements still quoted in our text-books on physiology. Moleschott gives the following table to show the daily average of the ingesta, and the proportion they ought to bear to one another.

Albuminates	130	grm.
Fats	84	"
Carbo-hydrates	404	"
Salts	30	"
Total solids	648	"
Add water	2800	"
Total ingesta	3448	"

Proportion of solids to water, 1 : 4.32.
Proportion of albuminates to fats and carbo-hydrates, 1 : 3.75.

Another mode of reckoning enables us to compare the amount of nitrogen with the amount of carbon taken into the body. The amount of the nitrogen in the daily food of an adult is about 20 grm.; that of the carbon, about 300 grm. The ratio of nitrogen to carbon is thus 1 : 15. But this way of reckoning is, undoubtedly, inferior to that previously adopted, for it is by no means a matter of indifference whether the carbon be taken in the form of fat or in that of albumen, the nitrogen in the form of albumen or in that of gelatin, etc., these important points being left altogether out of account in the latter mode of computation.

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[1] Physiologie der Nahrungsmittel. 2te Aufl. Giessen. 1859, p. 216.

No absolute and universal rules can be laid down concerning diet. Every individual must be fed (independently of certain outward conditions, to be referred to afterwards) in conformity with his or her age, sex, constitution, etc. During infancy and childhood, the growing organism—if this is to escape anæmia—must be furnished not merely with a larger relative supply of food than is required in adult life, but with a far greater proportion of plastic material (albumen) to subserve corpuscular proliferation. Hence, the normal ratio of albumen to other food-stuffs must be fixed at 1 : 4 for the period of growth, and the relative sum total of the ingesta during the sixth year of life must be about three times, during the eleventh year about twice as great as in the adult, to be in all respects satisfactory.

Mosler's experiments and observations have enabled him to calculate the total amount of the daily ingesta (including water) per kilogramme of body-weight as follows, for different ages:

Age. (Male sex).	Relative quantity of ingesta (in grammes).
6 years.	144
11 do.	115
18 do.	79
21 do.	71

If we assign $\frac{1}{20}$ of the body-weight (50 grm. per kilogramme) as the normal standard of the ingesta in adult life, and express this standard as unity, we get the following series of ratios:

[6] [11] [18] [21]
2.88 : 2.3 : 1.6 : 1.4 : 1.0

(The figures in brackets denote different ages.)

We know from experience that men require more food than women, both absolutely and relatively; the former owing to their larger size, the latter owing to the greater activity of their vital processes. Want of food produces actual disease more quickly and more easily in men than in women. In order to prevent anæmia, men require to be more liberally fed than women, though we are still in want of precise data concerning the average amount of ingesta in the two sexes compared with each other. I need hardly point out that pregnancy and lactation, conditions peculiar to the female, render an increased supply of nourishment urgently necessary. Should this fail, anæmia is certain to result.

Again, the quantity of food required depends, to an extent which has not hitherto been adequately realized, upon individual constitution. A vigorous organism demands a relatively large supply of nourishment in order to maintain its vigor; molecular metamorphosis is usually active, the current of the vital processes flows rapidly. Persons of relaxed habit, on the other hand, are better able to bear privation, and do not begin to exhibit any marked falling off in their already limited capacity for exertion till some time after their diet has been restricted. Lastly, persons of an irritable and anæmic temperament require a relatively abundant supply of nourishment to prevent their small store of blood from sinking below the level of health, owing to the demands made upon it by their tissues. These hints are enough to indicate that a person who is "healthy"—in the vulgar sense of the term—must, if he is to continue healthy and to escape anæmia, be provided with a quantity of food proportionate to the special requirements of his constitution. Hence, it is obvious that any attempt to fix the quantity and quality of the daily *menu* according to strict rule must prove a failure.

Lastly, the amount and kind of food required by the organism depend upon its environment. For instance, the diet-scale must be raised in winter and in a cold climate, the augmentation being chiefly in fats, carbo-hydrates, and other readily oxidizable materials suited for heat production. Continued exertion, too, claims an increased supply of nourishment; an abundant allowance of non-azotized food-stuffs, with a slighter increase in the albuminates, being required to maintain the needful store of energy in the blood. Finally, persons given to sexual excesses and debauchery require a very substantial dietary to enable them to indulge their vices with impunity; indeed, led by a just instinct, they generally make a wise selection from the bill of fare in the taverns they frequent.

The prevention of anæmia demands an adequate allowance of daylight and fresh air. These are important elements of physical well-being and promote sanguification. A life spent in close rooms, especially sunless workshops, brings on anæmia. It should be avoided on sanitary grounds by every one, so far as climate and occupation permit. These causes of anæmia are usually associated with a third, viz., insufficient exercise, protracted bodily quiescence being one of the obstacles to active sanguification (p. 316). A suitable amount of exercise in the open air should be taken daily with a view to health, if not already enforced by the nature of our occupation. It is a powerful means of preventing anæmia, and should always be ordered by the physician when the patient fails to take the initiative. Pecuniary reasons unfortunately do not always allow us to check anæmia at its source. Many people are obliged by dire necessity to spend their lives in sedentary work in-doors, and thus to injure their health. Public and private beneficence can do more to remedy such evils than medical advice. On the other hand, the physician must recommend, and if need be, enforce a complete change in the habits of such persons as voluntarily subject themselves to the risk of becoming anæmic by neglecting the conditions that are essential to the normal activity of sanguification, viz., light, air, and exercise. Scholars in easy circumstances, brooding all day long over their books—ladies, who when at home can scarcely muster the energy required for needlework or a novel, and whose acquaintance with the outer world is kept up through their carriage windows—to these and others like them a daily dose of fresh air and exercise apportioned to their strength (not necessarily in the form of hewing wood or drawing water) may be beneficially prescribed. It is in childhood and youth that the lack of light, air, and exercise is most injurious, for the growing body demands the utmost activity from the process of sanguification. In early life, therefore, prophylactic measures in this direction ought always to be adopted, especially if the individual type of constitution be already stamped with a disposition to anæmia and debility, or if growth be unduly rapid. How often in cases of this sort do we find even school injurious. We find it necessary to protest against the long hours passed in enforced quiescence in crowded class-rooms, against the habit of giving children long tasks to be performed at home, etc. Should the unlucky child show any signs, real or imaginary, of an inborn talent for art, this talent is forthwith developed (*e. g.*, by lessons and practice on the piano) till at length no time at all remains for rest, play, and exercise in the open air. Even the obligatory lesson in gymnastics on two afternoons a week is insufficient to counteract the bad effects of the educational system by which the child is deprived of leisure and fresh air. Should the physician perceive any signs of approaching anæmia in cases of this sort, he must urge upon the parents in the strongest terms he can command the necessity for restoring the proper balance between work and play—between intellectual development and bodily vigor. It is often judicious to send the child into the country now and then, as out-of-door exercise may thus be more readily obtained. I need hardly add that the grown-up person who accompanies the child will often reap much advantage from the change should his or her blood-making functions be impaired by an unsuitable course of life.

Undoubtedly beneficial as a certain amount of out-door exercise is for healthy persons, whatever their age, it is equally important that the muscular system should not, if possible, be overtasked. A vigorous constitution enables its possessor to undergo prolonged fatigue during the prime of life without ill effect, injury resulting only if other causes—especially want of food—contribute to produce it. Again, an over-anxious prophylaxis would often clash with the commands of duty, whose categorical imperative has obliged many a man, in season and out of season, to stick to his post and not to recoil from even "superhuman" efforts. But unless such heroism is morally justified by the importance of the end in view, even a man in the full enjoyment of his powers is bound to economize them and not to squander them prematurely without adequate reason. But as men who are absorbed into the vortex of a life, at once exciting and exhausting, are often wanting in prudence, it will often fall to the lot of the physician to warn them against their over-activity, to insist upon an alteration in their habits, and thus to prevent the occurrence of anæmia and debility. Protracted bodily exertion is most hurtful in the latter part of life, as the conditions requisite for the renewal of the blood and of its store of energy are least efficient in old age (p. 303). Old people, therefore, must beware of physical over-exertion, and persons who are very much occupied ought always to be advised to husband their strength more and more carefully as years go on. Unfortunately, the physician is often powerless to prevent the premature development of senile anæmia and marasmus, or to arrest their progress. Poverty is often to blame for people advanced in years having to exert themselves as strenuously as they did in youth, and to earn their bread in the sweat of their brow. This difficulty can only be met by public or private beneficence, which can seldom or never be depended on to interfere at the right moment. But over-exertion is also very dangerous for children and young persons who are growing, for the processes of growth absorb a great deal of the assimilated nutriment, the reserve of potential energy stored up in the blood being comparatively small. The state very rightly takes this into consideration, *e. g.*, in fixing the minimum age for military service. But there are no means of preventing unprincipled employers from subjecting children and undeveloped youths to continued over-exertion—true villeinage—shortening their due allowance of sleep, and thus barbarously robbing them of their youthful spirits and their health.

I have already pointed out (in the section on Etiology) how extremes of temperature, weather, and climate, may cause or promote anæmia. Every man is bound, by his own exertions or those of others, to shield himself against the hurtful influences in question by the needful provisions of house, clothing, etc. Of course, the best plan, when the health is in a precarious state, is to avoid the detrimental effects of a hot climate or a long winter by a temporary or permanent change of abode. This is particularly indicated in those cases where age, sex, and constitution are favorable to the development of anæmia, as for children and old people, for women and delicate persons. Thus, *e. g.*, parents whose duties (as missionaries, merchants, officers, etc.) oblige them to spend a great part of their lives in hot countries (British and Dutch India, Central America, Africa, etc.), do well to send their children home to Europe at an early age, so as to save their almost inevitable ill-health. So, too, the fashion prevailing in Central Europe, of spending the summer months in an Alpine region, is a wise precaution against anæmia, especially for women and children. Lastly, it is often very advantageous for delicate persons to winter in a southern climate, and thus to have an opportunity of enjoying sunlight and fresh air during the inclement season of the year without the risk of catching cold.

The connection that undoubtedly exists between anæmia and venereal excesses in the male sex renders it advisable to exercise due supervision over growing lads, and to recommend prudence to adults of dissipated habits. The physician is seldom able to offer any more direct opposition to an over-excited, precocious, or perverted sexual appetite. This difficult task must nearly always be left to parents and teachers, or to the personal initiative of those who are no longer under parental control. It is obvious that no general rule can be laid down as to the age at which sexual appetite may be regularly indulged without detriment to health, for, independently of bodily vigor, race, nationality, and climate produce considerable differences in this respect between different individuals.

Our preventive measures take a different form in relation to the sexual functions of the female. Here, of course, it is not so much sexual indulgence itself as its natural consequences—pregnancy, delivery, and lactation—that give rise to anæmia. Experience has proved that the worst effects of pregnancy and childbirth upon the composition of the blood are to be anticipated when the body has not yet reached maturity—when it still requires much blood to sustain its own growth and development. Early marriages, such as are common in large towns, and too often prompted by the desires of those concerned, are of doubtful wisdom from a medical point of view. Now and then the physician may be consulted by the bride's parents concerning the hygienic expediency of her approaching marriage; his answer must entirely depend upon the maiden's constitution and bodily development, and cannot be guided by any general formula. Many a vigorous and well-developed girl may unhesitatingly expose herself to the consequences of marriage, under the sky of Central Europe, on the completion of her seventeenth year; another, more delicately framed, will do wisely in waiting till she is eighteen or nineteen. The twentieth year once passed, matrimony may always be permitted in the absence of positive disease (especially of the lungs or heart). Under such circumstances, however, medical advice is not generally sought, the wedding being celebrated without any scruple as regards health. I have already had occasion to point out that pregnancy is a very fertile cause of anæmia; pregnant women ought, therefore, to be very careful in carrying out those prophylactic measures which have already been recommended, more especially as regards diet, exercise, and fresh air. Together with cheerfulness and a quiet mind, these precautions are enough to prevent a healthy woman, when pregnant, from losing her health and becoming anæmic. Finally, any intercurrent disease that may befall a pregnant woman should be removed as soon as possible, as it is very likely to prove the starting-point of anæmia; in cases of this nature, however, the anæmia is of a symptomatic and no longer of an idiopathic kind. The operative and dietetic measures to be adopted during and after delivery, in order to guard against excessive loss of blood, are fully described in works on obstetrics. Whether a healthy, though not actually robust, mother should evade the natural duty of suckling her offspring from fear of bringing on anæmia, is a question often submitted to the physician; he must be guided in his decision by the circumstances peculiar to the case. Mere delicacy of constitution on the mother's part does not contra-indicate lactation, so long as there is no special predisposition to disease (more especially to phthisis), and the appetite and digestive powers are unimpaired. If the nipples are in a suitable state, and the mammary glands capable of secreting a sufficient quantity of good milk, lactation ought to be unhesitatingly permitted. Under such circumstances we are often agreeably surprised to find delicate women, not previously remarkable for being full-blooded, not only able to meet all the phenomenal demands made upon them by their offspring, but actually gaining flesh, and to all appearance gaining blood as well. But if, as lactation goes on, the appetite and digestion begin to fail, it is prudent—if the mother's constitution be originally delicate—to wean the infant as soon as possible, since a rapid development of anæmic symptoms is otherwise almost certain to ensue. Again, it is not right for women who are not exceptionally robust to go on suckling too long, even though they may appear to bear the drain upon their constitution fairly well. No child ought to be kept at the breast after it is twelve months old. I may conclude my remarks on this subject by saying that every nursing mother requires continued and careful watching on the part of her physician, and the utmost prudence on her own part, in order that her task may be restricted within limits that are compatible with health.

The influence of prolonged and severe emotion in producing anæmia may, to a certain extent, be neutralized by conscious and energetic volition; the individual must obtain the mastery over the anxiety and grief that torture him. Original temperament often decides whether a man shall remain undaunted by the blows of fate, or be crushed and possibly destroyed by them. Persons of sanguine and phlegmatic nature are better off in this respect than those of melancholic and of choleric temperament; but the greater vigor of choleric individuals often enables them to rise superior to their misfortunes by self-appointed labor and new aims. It may occasionally be the physician's duty to rouse the energy of the will when it happens to be dormant. This may be done by manly exhortation, and by freeing the mind of the affected person from the exclusive tyranny of the emotions and turning it into some channel of useful activity. The measure of success attained will depend more on the art than on the professional knowledge of the physician; and only that physician deserves the name of a true artist who, without theatrical affectation and unctuous verbiage, combines an observant eye with a warm heart, notwithstanding the manifold hardening influences to which he is exposed.

The prevention of symptomatic anæmia is, in the first place, identical with that of the disease to which the anæmia is due. When any such disease, whether local or constitutional, is already present, we must aim at its speedy removal by appropriate interference. How this object may be attained in any particular case, and the likelihood of its successful attainment, will be found fully discussed in other parts of this Cyclopædia.

There, too, the reader may learn how the treatment of the primary disease, when local, is influenced by its situation; when constitutional, by its localizations. In this place, we can only suggest—from the stand-point of general pathology and general therapeutics—certain broad principles, varying with the nature of the primary disease, by conforming to which we may occasionally succeed in preventing the occurrence of anæmia.

The measures to be adopted for the prevention and arrest of bleeding from accidental wounds and during operations are fully described in works on surgery. Obstetric manuals treat of the methods of preventing and controlling hemorrhage before, during, and after delivery. Prophylactic measures are too often powerless against the bleeding that occurs in many internal diseases. Such bleeding is often unexpected and comes on during apparent health (*e. g.*, profuse hæmoptysis in commencing, but still latent, phthisis; hæmatemesis from a gastric ulcer, not hitherto betrayed by any symptoms). In other cases, a correct diagnosis may enable us to foresee the possibility of a dangerous hemorrhage. It then becomes our duty to counteract, as far as may be possible, the tendency to its occurrence; and the following suggestions are offered as a guide under such circumstances.

The bleeding that occurs during various internal maladies may be traced, partly to local or general disease of the vessels, partly to local or general rise of blood-pressure. Accordingly, when, in consequence of some disease, local disturbances have taken place in the nutrition of the vascular walls, there is a constant risk of rupture, bleeding, and consequent anæmia; we are then bound to take every possible precaution against mechanical injury of the threatened part, since this is not unfrequently the immediate cause of hemorrhage.

For instance, when an aneurism of the thoracic aorta has eaten its way through the ribs and is only covered by the soft parts, it is prudent to apply a leaden shield over the tumor so as to protect it against accidental rupture by external violence. Again, we prohibit hard and gritty articles of food in cases of gastric ulcer or of enteric fever with ulceration of the bowels, for fear of their injuring exposed vessels, and so giving rise to hemorrhage.

When the blood-vessels are diseased at any point, we must be on our guard against any rise of arterial tension, either general or limited to the affected area, for this may lead to rupture of the vessels whose power of resistance is impaired. A general rise of tension is brought on by any cause, such as a full meal (especially if it include hot food and drink, and alcoholic beverages), bodily exertion, passion, etc., which gives rise on the one hand to a sudden increase in the total volume of the blood, on the other to increased energy of the heart's action. Such patients ought, therefore, to cultivate peace both of mind and of body, to take their meat and drink cold—the latter in small quantities at a time—and to avoid alcohol, unless absolutely necessary to keep up their strength.

Local increase of tension may be caused by mechanical, chemical, and thermic irritation, either directly—as when an afflux of blood takes place to the particular vascular area; or indirectly—as when ischæmia of a neighboring vascular territory gives rise to collateral fluxion. Hence, a part from which bleeding may be expected to occur should be protected against any such direct irritation as might lead to its becoming congested. We must also take precautions against collateral hyperæmia of the affected region, and do our best to remove it by derivative means when it already exists.

Phthisical patients who show a disposition to hæmoptysis are exposed to risk by inhaling air loaded with dust, or containing acrid vapors, or of too high or too low a temperature; we know from experience that such causes are apt to provoke bleeding from the lungs. A draught of very cold water imprudently swallowed by such patients at a moment when the heart's action is excited, may cause an exhausting hemorrhage from the bronchi; the sudden chilling of the stomach causing ischæmia of its walls and thus determining a collateral fluxion to the respiratory organs (L. Hermann[1]). Again, it is very dangerous to go on with the cold-water treatment of enteric fever when the slightest trace of blood has been detected in the stools. The altered distribution of the blood consequent on the abstraction of heat (ischæmia of the surface, congestion of the internal parts of the body) is almost certain to cause profuse hemorrhage from the intestine.

Should the disease of the vascular walls be general instead of local—should there be a "hemorrhagic diathesis"—precautions of a local nature will clearly be useless. We must be doubly careful to avoid wounds and mechanical injuries, as well as all sources of irritation capable of exciting hyperæmia or increasing the energy of the heart's action; we must beware of anything likely to disturb the circulation, whether by collateral fluxion or by venous stasis. The remedies suited to improve the condition of the vascular walls will be discussed in the chapters on the treatment of Scurvy and Purpura.

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[1] Archiv f. die gesammte Physiologie, 1870. III. 8.

I need hardly point out that profuse bleeding, from whatever cause, should be checked as soon as possible. This is not merely a preventive of anæmia, but a principal element in its treatment; a prompt fulfilment of the *indicatio causalis* being the best guarantee of ultimate success.

Again, the means employed for the prevention of anæmia due to exhausting discharges—apart from those designed to stifle the primary disease—are identical with the measures by which we seek to fulfil the *indicatio causalis* and *indicatio morbi;* hence, their discussion may be reserved for the sections on treatment.

When the symptoms associated with the recent development of a tumor are such as to suggest that it is of malignant nature, it should be completely and immediately extirpated (provided its size and anatomical relations allow of the operation). We thus strike at the very root of the imminent cachexia and impoverishment of the blood. We must take care to do our work thoroughly, and not rest satisfied with the removal of those parts only which are visibly diseased. There is every probability that the surrounding tissues are already infected; hence, our incisions should be made well beyond the limits of the tumor, so as to enable us to remove its bed as well as itself. We must beware of permitting any shreds of the growth to remain in contact with the raw surface, for they may be grafted on to the healthy tissues, renew the morbid process, and ultimately necessitate fresh and still more extensive attempts at removal. Only when these and similar precautions are attended to, is the removal (for prophylactic reasons) of cancerous growths justified and likely to do good; it is equally clear that operative interference, when inadequate, is worse than useless.[1]

Those forms of oligæmia which result from toxic and infective processes, and those due to animal parasites (*anchylostomum duodenale*) can only be prevented by carrying out the measures described in the corresponding chapters of this Cyclopædia, and which may be grouped under the following heads: annihilation of the specific cause of disease; prevention of its access to the body; diminution of individual susceptibility to its influence.

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[1] *Waldeyer*, Sammlung klinischer Vorträge (*R. Volkmann*), No. 33.

I have already noticed the important part played by hindrances to the ingestion, digestion, and assimilation of food in causing anæmia. Continued attention to these functions, both in health and disease, must therefore constitute an important element in our prophylaxis; and remedial measures ought always to be resorted to as soon as the regular course of these physiological processes is interfered with by disease. The timely removal of any such disease is undoubtedly the surest way of preventing the development of a secondary anæmia. We must spare no effort to secure this object, when the disease is in any way amenable to treatment, and especially if it admits of being wholly eradicated. When this is impossible, we must confine ourselves to supplying the blood with as much material, charged with potential energy, as we can; and we must take care to supply it in the most appropriate form and by the most suitable channels. But these rules apply as well to the treatment as to the prophylaxis of anæmia; indeed, they are more important in relation to the former than to the latter; hence, any detailed discussion of the subject may be postponed.

Patients suffering from venous stasis due to disordered action of the heart are in imminent danger of becoming anæmic, since the circulatory disturbance interferes with the passage of the recrementitial lymph into the blood. Hence, the prophylaxis of anæmia in the presence of any primary disease tending to produce degenerative changes in the heart (more especially valvular defects, pulmonary emphysema, chronic interstitial pneumonia) implies the avoidance of everything likely to promote those degenerative changes, and thereby to augment the functional inefficiency of the heart. I refer to bodily over-exertion, exhausting emotions, intercurrent disease (especially of a febrile kind), and—in the female sex—childbirth. In our treatment of the primary disease and of its intercurrent complications we must never forget the patient's liability to "cachéxie cardiaque" (p. 335); all weakening measures, especially bloodletting, must be sedulously avoided, or only resorted to for the purpose of saving life. Lastly, when the signs of disturbed compensation are already developed, we must endeavor, as far as we can, to regulate the circulation by the periodical use of cardiac tonics—especially digitalis—in order, if possible, to delay the ill effects of the venous stasis upon the composition of the blood.

Prophylactic measures are altogether powerless against those highly malignant forms of anæmia which arise in connection with hypertrophy of the spleen and multiple disease of the lymphatic glands (splenic and lymphatic anæmia); for the etiology of these affections of the cytogenic apparatus is still shrouded in obscurity. Even after the diseased condition of the spleen and lymphatic glands is manifestly present, the threatened inanition of the blood does not usually admit of prevention; all that we can do is, by a tonic plan of treatment, to retard its course.

Finally, the prophylaxis of anæmia is very specially concerned with all pyrogenic noxæ. Aided by the thermometer, we have to recognize the presence of fever, and to oppose its progress with all the means in our power. We know that the chief causes of fever are: the entrance of infective material into the blood; the inflammation of parts abundantly supplied with lymphatics; the absorption of the products of previous inflammatory changes. Hence the preventive measures to be adopted against the consecutive form of febrile anæmia must consist, according to the nature of the particular cause, now in precautions against the contagia and miasms, now in prudent antiphlogistic measures, now in the timely removal (especially by operative interference) of stagnant inflammatory products. Recent clinical observations have proved that many fevers are avoidable, and that, by adopting suitable prophylactic measures, we may, in many cases, prevent both the fever itself and the anæmic marasmus which invariably follows it.

A few illustrations will help to impress the general principles stated above upon the reader's mind. The very successful results obtained since Lister recommended the strict fulfilment of the antiseptic method (careful purification of instruments and dressings, performance of surgical operations under carbolic spray, etc.) have taught us that both simple traumatic fever and malignant septicæmia are, in all likelihood, avoidable accidents—at any rate, in connection with recent wounds due to operation, or older wounds unattended by pyrexia. For instance, in the surgical wards at Basle, Lister's method has gradually been introduced, and carried out more and more carefully, during the last two years, and during this period fever has been noticed in less than one-third of all the patients admitted. This statement includes the slightest febrile exacerbations (rise of temperature to 38° C. = 100.4° F.) and the most severe injuries (compound fractures, etc.) and operations (ovariotomy, amputation through the thigh, etc.). Again, every physician is aware that the customary treatment of inflammation in all the manifold inflammatory disorders of various organs—by local bloodletting, application of cold to the inflamed region, preparations of iodine and mercury, both outwardly and inwardly employed—frequently produces antipyretic as well as antiphlogistic effects. This shows that many forms of fever depend on the presence of inflammation. Lastly, there are many cases in which fever is associated with the retention of inflammatory products in the body (serous and especially purulent exudations), disappearing at once when an abscess is opened or an exudation removed by tapping. Here, as in the other instances I have quoted to illustrate my meaning, the successful prevention of fever, or the early removal of its cause when it already exists, are measures of an eminently conservative kind, saving the blood from otherwise unavoidable impoverishment, and the organism from a reduction of its *status quo*.

I need hardly say that, for the prevention of anæmia and marasmus, it is quite as important to cure the fever as to remove its cause; but, as the means we employ for this purpose are, in the main, identical with those we have recourse to in the treatment of febrile anæmia, their description may fairly be reserved for the ensuing section

Indicatio Causalis.

A thorough inquiry into the causes of an existing anæmia usually constitutes an indispensable preliminary to its satisfactory treatment. Only by taking the patient's history and present condition into account, together with all the circumstances of his case, can we hope to unravel the tangled skein of causation sufficiently to enable us to frame a plan of treatment, whether empirical or rational, on an approximately secure basis. Moreover, there are many cases of comparatively recent origin in which a successful result may be achieved by simply fulfilling the *indicatio causalis*, without recourse to strictly remedial measures.

Should the negative result of an objective examination enable us to conclude that the anæmia is not symptomatic, should the patient's history indicate that the disease is idiopathic, our first aim in treatment will be to effect a complete alteration in his mode of life. A liberal supply of nourishing food must be substituted for comparative starvation; the pale recluse must be made to take out-door exercise; the victim of over-work and worry must be set free, either permanently or for a time, from the bondage of society; he must have peace of mind and sleep. These and similar measures are more likely to be successful than any "tonics," if, while the latter are administered, the patient is permitted to continue his previous mode of life. I need not recapitulate all those rules which have already been enumerated under the prophylaxis of idiopathic anæmia. Suffice it to say that the directions concerning individual noxæ, laid down for the prevention of anæmia, apply with still greater force to its treatment when they happen to meet the *indicatio causalis* in any concrete instance.

The treatment of symptomatic anæmia, on the other hand, will primarily consist in the removal, or, at any rate, the improvement and modification of the primary disease in which the blood-change originates, and by which it is kept up. The *indicatio causalis*, as regards the consecutive anæmia, will thus be identical with the *indicatio morbi*, as regards the primary disease. To some extent, moreover, a symptomatic treatment of the latter will tend to suppress the causes of the former, for the effect of a morbid process in causing anæmia often depends, not so much on the totality of its essential characters, as on some particular, perhaps accidental features; hence, we may frequently find ourselves most successful in checking the progress of anæmia when we turn our attention, chiefly or entirely, to the latter. I shall now briefly recapitulate the various causes of symptomatic anæmia—still from the standpoint of general pathology,—laying down suggestions for their suitable management as I go on. Most of the subject-matter has already been dealt with in the foregoing section; I shall therefore lay particular stress on those points which have not hitherto received due consideration.

The *indicatio causalis*, as regards anæmia produced or kept up by hemorrhage, consists in stopping the effusion of blood as speedily as possible. The surgical and obstetrical aspects of this problem, together with a description of the styptic methods in ordinary use,[1] need not engage our attention here. Treatment is often powerless against the bleeding that occurs in the course of various visceral diseases, especially when the blood is poured out internally. The prospect is less desperate when the bleeding takes place from a part accessible to styptic applications, *e. g.*, the lining membrane of the nasal fossæ. Such applications ought to be made at once—cold, plugging of the nares, alum, liquor ferri perchloridi, and the mineral astringents generally, being employed. At the same time the precautions enumerated in the section on prophylaxis (p. 434)—avoidance of bodily exertion, of mental emotion, of hot food, of alcoholic beverages, etc. —must be strictly observed. Lastly, the reader may be warned against removing the plugs and other means of compression employed, roughly and incautiously, and thereby disturbing any coagula that may have formed. If the blood be poured out from some organ or region in the interior of the body, our prospects of checking the hemorrhage by any direct method are far slighter; yet even in these cases we must not omit to employ any means capable of moderating the bleeding, whether mediately or immediately. Keeping body and mind at rest, avoiding all food and drink likely to excite the heart, removal of hurtful sources of irritation, stopping all treatment calculated to induce or maintain direct or collateral hyperæmia of the bleeding part—these are negative but highly important measures. Cold ought to be energetically applied to the surface, as near the supposed seat of hemorrhage as possible, by means of ice-bags, cold compresses frequently renewed, etc. Should the blood come from any point that is accessible to astringents, these ought always to be employed, with the proviso that their employment do not cause the patient bodily discomfort or excite his mind.

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[1] Ligation of bleeding vessels; compression by the fingers, by instruments, by bandages; plugging; local application of cold and of the actual cautery: local application of styptics and astringents to the bleeding surface, etc.

Thus, *e. g.*, when bleeding occurs from the stomach and bowels, alum whey should be liberally administered; when from the former alone, solutions of tannic acid or nitrate of silver. In copious and obstinate hæmoptysis, inhalation of atomized solutions of perchloride of iron or of alum should be tried. In hæmaturia large doses of tannic acid may be given internally, as this substance is eliminated by the kidneys in the form of gallic acid. In bleeding from the rectum and colon, astringent enemata are indicated. Concerning the dose and mode of administration of these different remedies, the reader will obtain full information from those chapters of the present Cyclopædia which treat of hemorrhage from the different organs of the body.

Remedies which tend to cause contraction of the vessels are occasionally of great use. Among them the preparations of lead and of ergotin occupy a prominent place. Acetate of lead may be given in a dose of 0.3 grammes (four and a half grains) several times a day, in powder or pill; or the watery extract of ergot in large doses from one to three times a day (0.2–0.5 grammes [from three to eight grains] by the mouth, or better still, hypodermically). The occurrence of the well-known symptoms of poisoning (sensation of woolliness in the finger-tips, slow pulse, nausea, colic, etc.) contra-indicate the further use of these remedies; but we must not allow ourselves to be deterred from a methodical employment of the large doses indicated above by over-anxiety as to the consequences.

When anæmia is kept up by pathological discharges, the topical application of astringents and balsamic remedies to the secreting surface is urgently indicated. Such remedies will often put a stop to the discharge. I may instance the treatment of bronchorrhœa by inhalations of tannic acid and alum or of the vapor of turpentine; the treatment of genito-urinary discharges by the internal administration of tannin, cubebs, copaiba, and by the injection of astringent solutions into the urethra and bladder. The anæmia caused by acute inflammation with abundant exudation is best counteracted by antiphlogistic measures; that resulting from ulceration and necrosis of tissue should be treated, *i. e.*, should have its causes eradicated, by surgical interference. In the anæmic marasmus caused by heterologous growths of a malignant character, the *indicatio causalis* can only be met when the tumor admits of being extirpated without immediate danger to life. It is very doubtful whether condurango bark, lately vaunted as a panacea for cancer, exerts any influence when administered internally. In removing malignant growths by operation, the precautions enumerated on p. 435 require a double share of attention when symptoms of anæmia and marasmus are already present; for it is under such conditions that the disease is most likely to recur. When the malignant process has already become generalized, the extirpation of a single tumor is only indicated when it happens to interfere mechanically with some vital organ; otherwise its removal is useless, and should not be attempted. A systematic excision of all the growths accessible to the knife in cases of generalized carcinosis and multiple sarcoma offers no guarantee against the development of similar tumors in the interior of the body; moreover, it is often impracticable. The complete and early removal of the primary tumor, when its position allows of it, is the only effectual safeguard we can offer; I need only, therefore, recommend the remarks on p. 435 once more to the consideration of the reader.

In the toxic and infective forms of anæmia, it must be our object to promote the elimination or destruction of the poison which has entered the body. Here are some examples of the success that may attend the fulfilment of the *indicatio causalis* in cases of this nature. The methodized administration of quinine, arsenic, and the preparations of eucalyptus gives brilliant results in the treatment of the paludal cachexia. Mercurial inunction, prudently carried out, exerts a positively tonic influence in cases of syphilitic marasmus. These instances prove the efficacy of specific treatment directed against the specific causes of particular varieties of anæmia. The anæmia due to animal parasites, too, can only be cured by employing suitable anthelmintics.

In the management of *Anchylostomum*-disease in Egypt, Griesinger obtained very successful results from the use of oil of turpentine in combination with calomel, in purgative doses. Wucherer mentions that the milky juice of a plant growing in Brazil (*Ficus doliaria*) is popularly—and successfully—employed as a remedy for the same disease.

Diseases that induce anæmia by interfering with the ingestion of food are of so many different kinds that no general rules can be laid down for their treatment. The reader may consult those chapters of the present work in which the diseases of the upper part of the alimentary canal (mouth, pharynx, œsophagus, stomach) are dealt with ; I need only say that when local obstacles in that region, *e. g.*, inflammation, ulceration, stricture, paralysis, interfere with swallowing or with the passage of the stomach-tube, excellent results may be achieved by adopting Leube's method. This consists in administering a mixture of raw meat and pancreatic tissue per rectum. (For details, see article on Diseases of the Stomach.) This plan of artificial feeding is also of inestimable value in that form of anæmia which results from uncontrollable vomiting. In many such cases admitted into the clinical wards at Basle during the last two years, the introduction of food by the mouth has been reduced to a minimum or even wholly stopped for days without giving rise to any appreciable symptoms of inanition so long as the patients were fed by the bowel. It was often found, moreover, especially in cases of gastric ulcer, that after several days of absolute rest the stomach would regain its tolerance of food ; in all likelihood because the ulcer underwent spontaneous cicatrization during the interval, and the cause of vomiting was thus removed. The following is a brief account of one of these cases :

Marie J . . . ., thirty-six years of age, a cook, admitted on 3d of November, 1874. Has suffered previously from occasional attacks of cardialgia, but without vomiting. Enjoyed good health during the summer of 1874. Since the beginning of October, however, has been subject to severe cardialgia with intense though circumscribed tenderness on pressure over the epigastrium. During the last fourteen days has been sick several times a day; the vomited matters have always been very acid, and, on one occasion, they contained blood. On November 3d everything she took caused acute pain, and was immediately vomited. From the 4th to the 13th, accordingly, her stomach was kept absolutely at rest, and during this period an enema of pancreatic mince-meat was administered daily (70 grammes of pancreas, 140 grammes of meat). No return of sickness or cardialgia after the 4th. The patient feels perfectly well, shows no intolerance of the enemata, the residue of which has generally to be cleared out by an evacuant clyster after twenty-four hours' sojourn in the rectum. On the 13th of November a milk diet in gradually increasing quantities is begun. No further treatment. Discharged cured on 3d of December, 1874.

If anæmia be caused and maintained by exhausting diarrhœa, we must have recourse to astringent remedies, and to those which, like opium, ipecacuanha, and acetate of lead, apparently owe their constipating property to their power of retarding or arresting peristalsis, and thus preventing the chyme from being hurried too rapidly down the digestive tube. Again, should we have reason to suspect that the exaggerated peristalsis is excited by some acrid products resulting from decomposition of the intestinal contents, our best plan, in order to stop this so-called fermentation-diarrhœa, will be to prescribe antizymotics, *e. g.*, small doses of calomel, creosote, benzine, etc.

The most common of all the varieties of symptomatic anæmia is that resulting from dyspepsia—from some disturbance in the chemical processes of digestion. Diminished secretion of the peptic juices, often associated with the formation of a thick layer of viscid mucus adhering to the lining membrane of the alimentary canal—imperfect transformation of the ingesta into those products of hydrolytic decomposition (peptones, sugar, etc.) which are readily capable of being assimilated—abnormal changes (due to fermentation and putrefaction) in the non-assimilated residue of the intestinal contents, with the formation of new products which irritate the mucous membrane and give rise to dyspepsia—such are the principal links in the chain of hostile influences which it is our object to break through, or cautiously to unloose. For thus alone (and not by merely fulfilling the *indicatio morbi*) can we hope to overcome the secondary anæmia developed in such cases ; it is in these dyspeptic forms of symptomatic anæmia that the immense importance of attending to the *indicatio causalis* is most clearly manifested. I cannot enter here upon the treatment of dyspepsia in all its varieties ; besides, the subject has been exhausted in other volumes of the Cyclopædia (Diseases of the Digestive Apparatus). Still, its vast importance in relation to anæmia obliges me to allude to a few principles which underlie the rational treatment of dyspepsia. The line to be adopted in any and every case may be clearly pointed out, though of course it may not be always possible to follow it out to the desired issue. The following are evidently the chief objects to be kept in view :

I. Arrest of all abnormal processes of decomposition in the digestive tube, and expulsion of all fermenting and putrefying ingesta.

Whether this object may be best attained by the administration of antizymotic remedies, combined with the utmost possible restriction as to food, or by the direct evacuation of the stomach by means of the stomach-pump and emetics, or by a course of laxatives, will depend on the nature of the disease and the special circumstances attending it in any particular case. I need not discuss the question here.

II. Rousing the digestive surfaces to pour out a normal secretion, and cleansing them from adherent mucus.

This may be satisfactorily effected, in the majority of cases, by means of alkaline and saline carbonated waters (Carlsbad, Vichy), or by artificially prepared solutions of the corresponding salts. The dose must, of course, be regulated in accordance with the (confined or relaxed) state of the bowels. The digestive functions may be stimulated in a similar way by many of the preparations of rhubarb, especially by the "*Tinctura Rhei aquosa*" administered several times a day in doses of 5 grm. for a considerable period. The more advanced the consecutive anæmia, the more useful is the substitution of the alkaline-saline chalybeate waters of Franzensbad, Elster, Kissingen, and the iron-water of Tarasp, for the alkaline and saline carbonated waters and their artificial congeners. The nearer the digestive trouble approaches the type of simple atonic dyspepsia—the more decidedly it manifests itself, not as an absolute intolerance of all food, but as an intolerance of large quantities of food—the more benefit may be anticipated from the administration of the simple or aromatic bitters, or of the strictly tonic preparations of iron. The action of the latter will be more fully considered when I come to speak of the *indicatio morbi;* so much, however, may be said here that, while they are of marked efficacy in simple atony of the digestive organs, they should, as a rule, be avoided in true dyspepsia (using the word in its narrower sense to denote qualitative faults in the chemistry of digestion). Finally, I may repeat that these remarks are only meant to *suggest* the line of treatment in the dyspeptic and apeptic forms of anæmia; for information as to the mode of carrying the above principles into practice, the reader must consult those chapters of the Cyclopædia which are devoted to the diseases of the digestive system individually. Accordingly, I need not enter on any speculations about the way in which these various methods are supposed to act, or discuss the pharmaco-dynamics of the different remedies I have enumerated.

In the "cardiac cachexia," the *indicatio causalis* points chiefly to the necessity for restoring the enfeebled energy of the heart as the prime cause of the venous stasis. The appropriate remedies are cardiac tonics in the narrow sense of the term, viz., digitalis (p. 437), and general tonics in combination with a strengthening diet. As regards the latter, the *indicatio causalis* is identical with the *indicatio morbi.* In the splenic and lymphatic forms of anæmia, so hopeless from the point of view of prognosis, arsenic (given in Fowler's solution by the mouth or hypodermically, in gradually increasing doses) seems to deserve more confidence than any other of the remedies that have been proposed (Czerny, Mosler, Winiwarter, and others). Further observations are needed to show how far we may be justified in regarding arsenic as a specific for malignant lympho-sarcoma.

In febrile anæmia, the *indicatio causalis* is met by treatment of the febrile process. Of the various antipyretic measures which have lately been employed with great zeal and success, those alone are deserving of notice at our hands which are not merely designed (like the cold-water cure) to combat the symptom "heightened temperature" with its physical opposite—cold—but which are intended to repress the fever itself, the *cause* of the abnormally heightened temperature. The chief antipyretics employed for the latter purpose are the preparations of quinine and digitalis, to which, according to the interesting observations of E. Buss,[1] salicylic acid may fairly be added. Without entering on a detailed consideration of the modern system of antipyretic medication, I may be allowed to formulate the main principles on which the treatment of the febrile process, as a means of combating febrile anæmia, rests. I shall also enumerate the measures which experience has shown to be effectual for this purpose. The following are the chief points at which we ought to aim in our treatment of the febrile state:

I. To convert fever of a continuous or sub-continuous type into fever of a remittent or, if possible, intermittent type.

This purpose may often be satisfactorily attained by the administration of a single large dose of quinine (Liebermeister), or of salicylic acid (Buss), repeated periodically. The dose of sulphate or hydrochlorate of quinine, which we are now in the habit of prescribing at the Basle Hospital in enteric fever, pneumonia, and other severe pyrexial diseases, varies according to the resistance offered by the fever, from 1.5 to 3 grm. (twenty-two to forty-five grains); that of salicylic acid[1] from 4 to 6 grm. (a drachm to a drachm and a half). In continued fevers, both of these remedies are usually administered towards evening, so as to make their antipyretic influence coincide with the normal tendency to a fall of temperature and diminished heat production; the effect produced is thus intensified (Liebermeister). The dose found to be effectual is repeated in twenty-four or forty-eight hours, according to the severity of the case; it is repeated again and again, at similar intervals, so long as the fever continues to exhibit a tendency to renewed exacerbation. Slight toxic symptoms (both drugs, when given in the above huge doses, cause ringing in the ears, dullness of hearing, and often slight nausea) are hardly ever absent; but they do not matter. The antipyretic effect is usually very striking, as may be seen from the annexed charts.

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[1] Ueber die antipyretische Wirkung der Salicylsäure. Inaugur. Dissertation. Basel, 1875. Cf. also Correspondenz f. schweizer. Aerzte, 1875. No. 11, 12, 13.

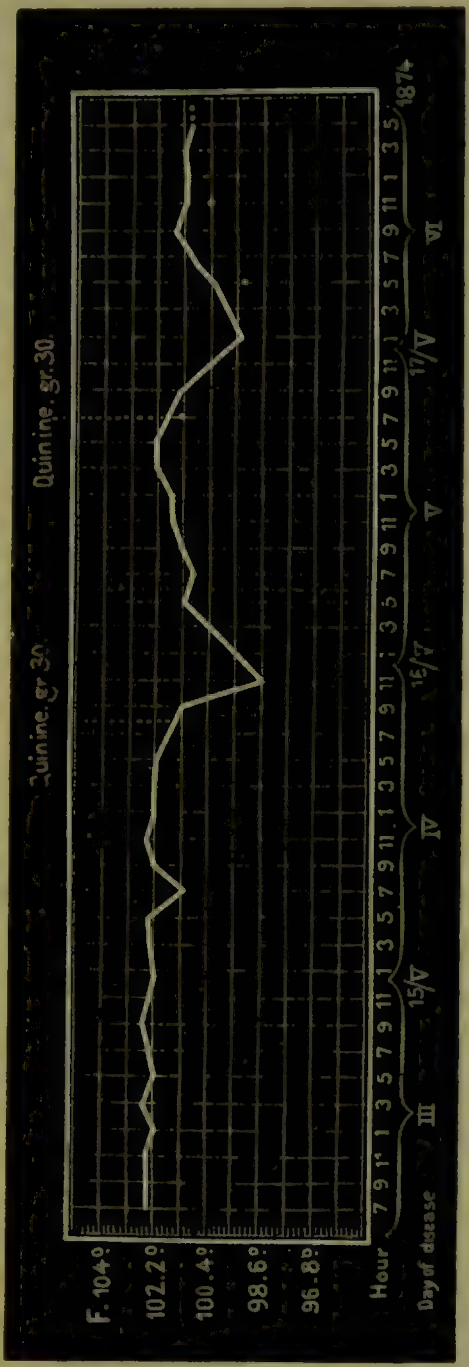

FIG. 1.

Fig. 1. N. S., a vigorous man of forty-five; lobar pneumonia; high continued fever. Morning intermissions artificially produced by quinine (Basle Hospital). Temperature taken every two hours in axilla.

Fig. 2. S. B., moderately strong man of forty. Very severe asthenic pneumonia, running a protracted course.

First week.—Treatment by salicylic acid; well-marked morning intermissions after every dose; the intermissions fail to occur when the drug is omitted (Basle Hospital). Temperature in axilla every two hours.

When the pyrexia is so obstinate as to resist single massive doses of any one antipyretic remedy, it may still be compelled to intermit by the administration of a series of doses of digitalis (given at short intervals, till the pulse is reduced in frequency) throughout the day, followed by a full dose of quinine or salicylic acid at night. At Basle, we generally use pills containing 0.05 grm. (three-quarters of a grain) of powdered digitalis leaves; one of these pills is given every hour throughout the day, and a dose of 2–3 grm. (thirty to forty-five grains) of quinine at night. The effect of this plan of treatment, in bringing down the febrile temperature in cases where quinine alone had been found unavailing, is well shown in Fig. 3.

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[1] Salicylic acid is best administered in wafers, according to the method of Limousin. Each pair of wafers contains 0.5 grm. (seven and a half grains) of the remedy: from 8 to 12 such doses must be taken in as short a time as possible—within an hour at the utmost.

Fig. 3. R. R., vigorous young man of twenty-two. Very severe and protracted attack of enteric fever. Quinine and cold baths were not followed by a sufficient reduction of temperature. Striking effect produced by the simultaneous administration of digitalis and quinine (Basle Hospital). Temperature taken in axilla every two hours.

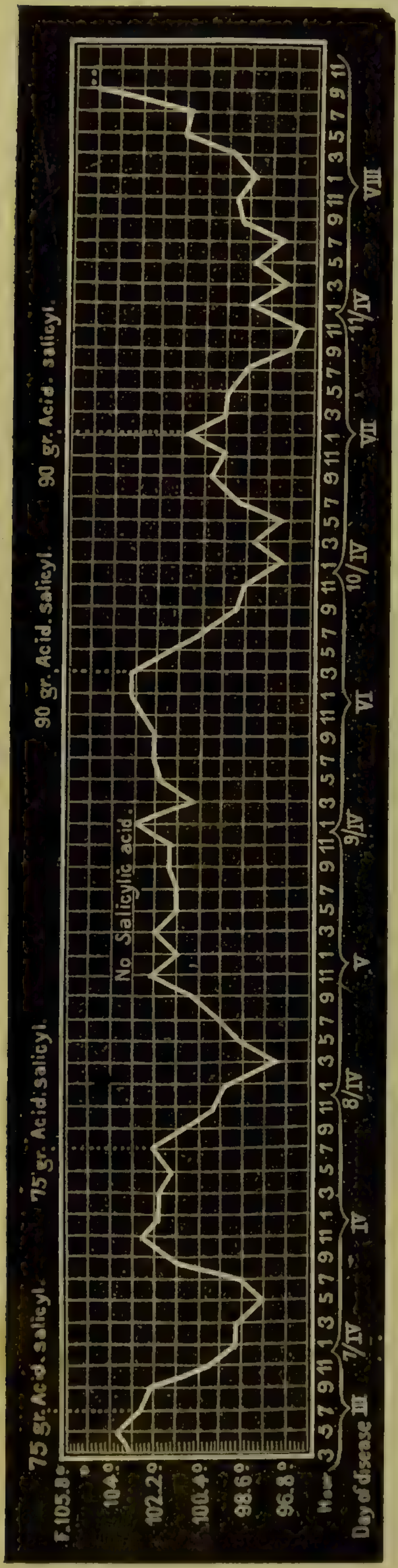


Fig. 2.

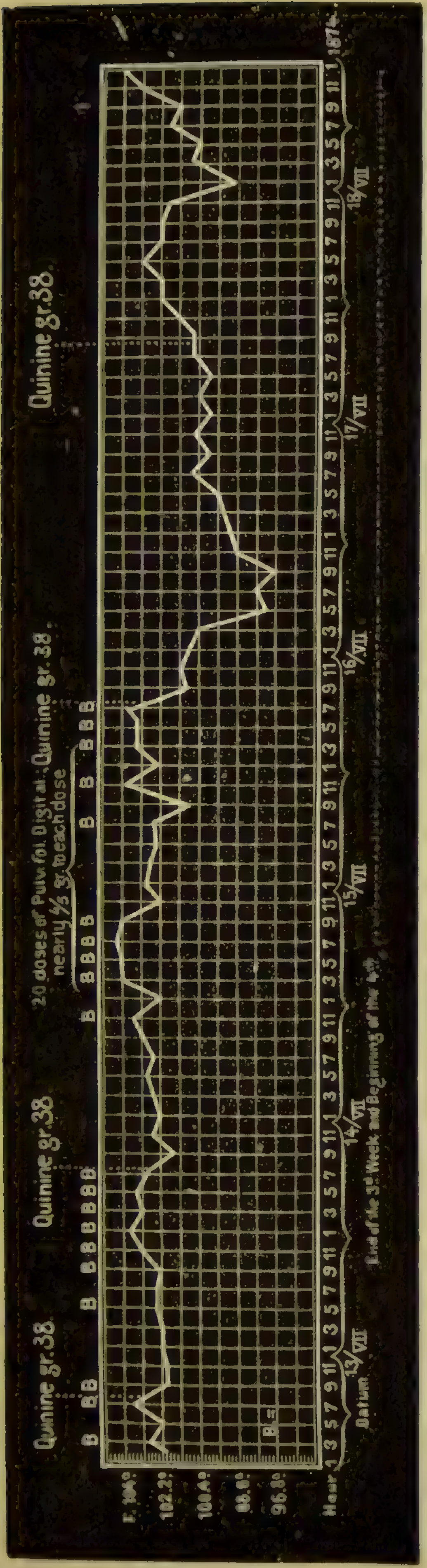
II. To suppress and moderate the exacerbations when the fever is of a remittent or intermittent type; even when this type has been artificially induced by the methods described under (I.).

When the fever normally exhibits evening exacerbations with morning remissions, a large dose of quinine or of salicylic acid given some hours before the onset of the daily exacerbation will often prevent its occurrence altogether; should it fail to do this, it will at any rate moderate the intensity of the exacerbation or shorten its duration. The dose is that specified under (I.); it should, however, be given during the forenoon instead of the evening. For an illustration of the antipyretic effect produced, see Fig. 4, the temperature-curve of a man suffering from pleurisy with daily intermissions of pyrexia.

Fig. 4. J. M., a moderately strong man of thirty-nine. Severe pleurisy, with copious effusion into the right side of the chest. The pyrexia intermits spontaneously every morning. Salicylic acid given at too late an hour on two successive days; antipyretic effect inadequate. The acid was afterwards given at the right time (from three to four hours before the setting-in of the exacerbation), and its antipyretic effect was complete (Basle Hospital). Temperature taken in axilla every two hours.

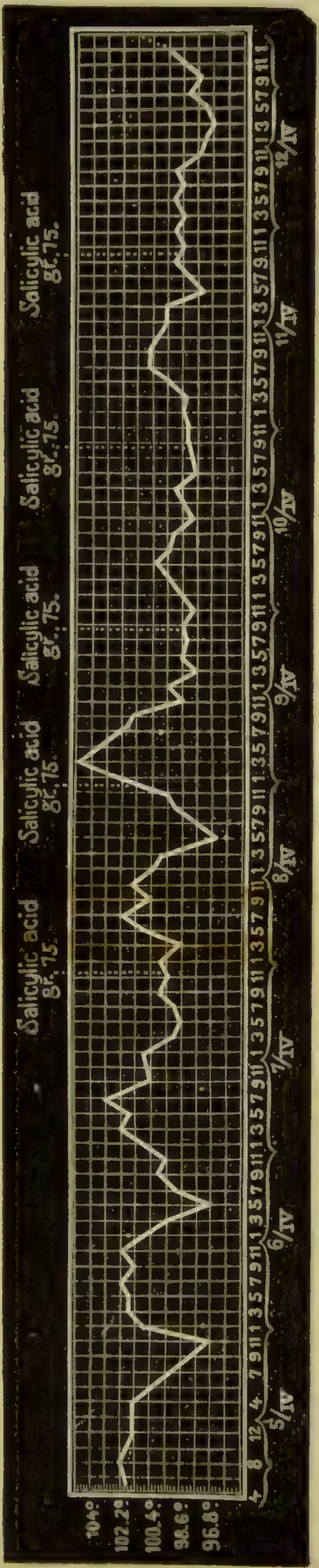
Should we be indisposed to repeat these mas-

FIG. 3.



B = Full bath, with water at a temperature of 68° F., and lasting ten minutes.

FIG. 4.



sive doses too frequently in cases of prolonged fever, owing to their unfavorable influence on digestion, we may administer them once in forty-eight hours instead of every day; eventually, an interval of several days may be permitted to elapse between successive doses. Should the evening temperature not rise to any excessive height, we may, instead of resorting to vigorous measures, content ourselves with prescribing smaller doses of quinine and digitalis several times a day until the evening exacerbations are allayed. The well-known pills of Heim and Niemeyer are very suitable for this purpose. (Sulphate of quinine, thirty grains; opium, ipecac, of each, seven and a half grains; extract of elecampane, enough to make twenty pills. From three to five pills to be taken daily.) These pills are extensively employed at the Basle Hospital. In cases of continued fever they may be given together with single massive doses of quinine or salicylic acid at night, so as not merely to obtain artificial intermissions of the fever, but also to lower the evening temperature; since we cannot venture to administer the above-mentioned huge doses of antipyretic remedies twice in the twenty-four hours.

Veratria has also been recommended as an antipyretic. It can only be indicated on very rare occasions. It causes far more gastric irritation than either quinine or salicylic acid; it is also liable to give rise to disagreeable attacks of cardiac paresis, with a permanent state of nausea and collapse. In my opinion, it may very well be dispensed with.

DS & WEST RIDING
CAL SOCIETY

Indicatio Morbi.

In the treatment of anæmia our first thought must always be directed to the fulfilment of the *indicatio causalis.* By removing the concrete causes of the malady we may often succeed in curing it without more ado. But there is a large number of cases in which the fulfilment of the *indicatio morbi* is at least as important as that of the *indicatio causalis.* This is especially true of the more extreme forms of the disease; a purely causal treatment of which is often extremely slow and very often unsuccessful. For in the debilitated organism the processes by which the blood, after the removal of the causes that have induced anæmia, is restored to its normal condition, are often unduly languid and restricted within narrow limits. Therapeutic interference of a direct kind is necessary to rouse them and to extend their operation; and there can be no doubt that a prudent use of measures immediately antagonistic to the impoverishment of the blood will often lead more quickly to the desired end than mere removal of the causes by which the anæmia has been brought on. Again, the fulfilment of the *indicatio morbi* is obligatory when that of the *indicatio causalis* is impossible. In such cases we must, of course, abandon all hope of lasting cure; but a continued renewal of the blood-store by artificial means will often enable us to maintain the patient's health and energy on a level which differs only in degree from that of genuine health.

The treatment to be pursued may be inferred from the general pathogeny of the disease, and is of a two-fold character. To promote sanguification, to preserve the organic *status quo* of the blood and tissues—such are the two aims to be pursued by a rational method of tonic treatment. The former must take the foremost place when the anæmia is due to inanition; the latter, when it is due to consumption; when the malady is of complex origin the two lines of treatment must be pursued together; in no case, however, ought either of them to be wholly neglected. Even if it were possible to divide the remedial measures about to be described, according to their mode of operation, into "true tonics," *i.e.*, aids to sanguification, and "conservative remedies,' I should not adopt this classification, for it would clash too forcibly with our conventional ideas concerning the natural connection between certain curative agents whose mode of operation is really quite distinct. Hence I shall keep to the usual division into "dietetic" and "medicinal" agents, adding a short account of transfusion as a third mode of treating anæmia. This voluntary neglect of the pharmacodynamic principle in our primary classification will render it necessary to bear it in mind all the more carefully when discussing individual methods.

The chief problem in the dietetic treatment of anæmic patients is that of suitable alimentation. Their food must, in the first place, be really nutritious, *i. e.*, it must contain a sufficiency of plastic material. Secondly, it must be digestible—not in a merely general sense, but specially adapted to the digestive powers of the individual patient. I have already pointed out that the body cannot dispense with albuminates—the plastic constituents of food—for any length of time; and they are yet more indispensable to the anæmic patient whose malady is largely due to hypalbuminosis. It would, however, be absurd to make anæmic patients swallow large quantities of albuminous matter at short intervals (say a beefsteak every two hours) with a view to supplying the deficiency as quickly as possible. On the contrary, we must always recollect what a large supply of digestive secretions (gastric juice, pancreatic fluid, *succus entericus*) is required for the assimilation of any considerable amount of albumen. Now the peptic secretions are scanty in the anæmic patient; in other words, he suffers from atonic dyspepsia. The undigested residue of albumen in his alimentary canal will speedily putrefy, and the products of its decomposition will set up catarrh of the gastro-intestinal mucous membrane. These considerations are enough to show that a wholesale administration of albuminous food to anæmic persons is out of the question. More especially must it be avoided in the dyspeptic forms of anæmia, when the disease is produced and kept up by disorders of digestion. In such cases the digestive apparatus often resents the introduction of albumen, and the smallest excess in this respect is dangerous, as every increase in the severity of the dyspepsia is attended by a corresponding increase in that of the anæmia. We may avoid these pit-falls, and yet supply the blood with a relatively large amount of albumen, by never over-loading the stomach with albuminous food at one time, but increasing the number of meals. Anæmic persons should, if possible, take albuminous food more often than those in health, but always in small quantities and in a digestible form. Should the atonic dyspepsia be severe we cannot be too careful in regulating the patient's diet; we must begin with very small quantities of food, increasing them gradually as his strength and digestive power improve. We must renounce all idea of supplying any large amount of albumen in a limited time; the meals must not at first be too frequent. Among the more digestible albuminous articles of diet may be enumerated: milk, lightly-boiled yolk of egg, roast chicken, capon, and turkey, boiled trout. At a later period game and dark meat of delicate fibre—such as venison—may be allowed. Soon, too, the patient will be able to eat lean ham uncooked, shavings of underdone beef slightly salted, etc., in small quantities. These articles will therefore find a place in the dietary of anæmic persons, particularly of those convalescent from acute disease. The diet must be varied and the caprices of the stomach attended to; even very digestible kinds of azotized food must be avoided, when the stomach happens to resent them, or when they fail to satisfy the palate. Thus we are often compelled to reject milk, otherwise so suitable, for some patients find it nauseous and others are unable to digest it; sometimes it causes catarrh of the stomach and intestines. Experience shows that unpalatable food is prone to disagree; the converse of this, however, does not hold good; for many a feeble invalid has sacrificed his stomach for the sake of dainties.

Finally, there are a few cases in which the presence of anæmic marasmus in an extreme form renders the introduction of plastic material absolutely essential, while the digestive powers are too feeble to cope with even the lightest of the azotized foods enumerated above, or the anorexia is so great as to inspire the patient with the utmost repugnance to taking nourishment. It then becomes our duty to relieve the digestive system of a great part of its work and to set aside the sense of taste. These objects may be attained by feeding the patient *per rectum;* Leube's pancreatic enemata, already alluded to, enable us to elude the palate and to give the whole of the intestinal tract, with the exception of its lowest section, a holiday. Assimilation, nevertheless, goes on uninterruptedly. Feeding by Leube's method is, of course, contra-indicated by the presence of diarrhœa; in many cases, however, the diarrhœa may be checked by opiates, etc., and when the storm of peristalsis has been allayed the rectum may be able to retain the nutrient mass. On the other hand, should the patient's appetite render it desirable to feed him by the mouth, while the atony of his digestive powers is too great to allow of his assimilating even such nourishment as milk, finely triturated yolk of egg, etc., we may have recourse to the *solutio carnis*,[1] prepared by Mirus, of Jena, in conformity with the instructions of Leube and Rosenthal. This is a preparation containing meat which has been artificially peptonized by being super-heated with dilute hydrochloric acid under pressure; it is not unpalatable, and its jelly-like consistency, together with the abundance of peptone it contains, renders it very easy of assimilation even in extreme apepsia. From 100 to 500 grammes may be given daily in gradually increasing proportions.

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[1] Vide note on page vi. of Volume XII.—Tr.

Many trials of this preparation, made both in hospital and private practice, have yielded very favorable results. In some cases it could not be taken, owing to a feeling of repugnance excited by its glutinous appearance and somewhat sickly taste. It should always be given in broth, or, as Leube suggests, with the addition of a little Liebig's extract to improve its flavor. Moreover, the patient must not be limited to it for any length of time; any sort of food, taken continuously, being apt to excite disgust. Lastly, its liability to undergo decomposition should always be kept in mind. It is sold in hermetically sealed tins. When a tin has once been opened, its contents must be consumed as fast as possible; for, especially in hot summer weather, the access of air may be followed by putrefaction in from thirty-six to forty-eight hours. As each tin holds 250 grm. of the solution, several patients in a hospital may be made to share it, when the quantity required for each of them is small.

Even in the febrile variety of anæmia the existence of pyrexia must not prevent us from giving albumen in small quantities, and in a digestible form. When the temperature is high, albuminates are very imperfectly assimilated (p. 338); hence, fever patients must be fed with great prudence. Under no circumstances—however much the increased consumption of the tissues may tempt us in that direction—ought a "substantial" diet, *i. e.*, albumen in considerable quantities, and in a form not easy of digestion, to be allowed when the symptoms of dyspepsia are well-marked. The plastic material required for the reconstruction of the tissues should be given in small quantities, frequently repeated; it should be given in some very digestible form. These requirements are, to some extent, fulfilled by milk and yolk of egg, beaten up in broth, wine, or brandy; they are still more perfectly fulfilled by the fluid meat described above. It may be laid down as a rule that in protracted fevers, when the progressive consumption of the albuminous tissues renders it imperative to make good the waste, however imperfectly, we ought cautiously to administer as much albumen in a suitable form as the patient is able to assimilate (Uffelmann[1]). It is quite a mistake to deprive a fever-patient altogether of albumen on the ground (true as it is) that the metamorphosis of azotized matters in the body is accelerated by the introduction of albumen into the system, and that the already excessive decomposition of albuminous matters may thus be still more increased. It is quite true that the metamorphosis of nitrogenous compounds is always increased by introducing more nitrogen into the body. We know that even in healthy persons the elimination of urea varies with the quantity of albumen in the food. Hence, the very same objections that have been urged against giving albumen in fevers might be urged with equal force against giving it in health. But as a larger proportion of albumen in the diet of a healthy person, though followed by an increased elimination of urea, does not cause wasting of the body, so, in fever, there is no reason why giving albumen should increase the waste of the tissues. The absolute quantity of nitrogen excreted in fever proves nothing concerning the amount of "organ-albumen" decomposed; it is only the difference between the intake and output of nitrogen that enables us to judge of the waste of "organ-albumen" going on. But no evidence has yet been brought to prove that giving albumen can disturb the nitrogen-equilibrium of fever-patients in a greater degree than it is already disturbed by the fever alone. Hence, there can be no theoretical objection to administering albuminous food, in a digestible form, to patients suffering from fever.

The following table, taken from the work of Huppert and Riesell, will serve to confirm the above statements. It throws a flood of light on the points we have been considering, by giving us the total intake and output of nitrogen, with the difference between them, in a fever-patient subjected to varying conditions as regards the supply of albuminous nourishment (meat).

A man, aged thirty-one, convalescent from enteric fever, and suffering from caseous pneumonia. The fever lasted, with slight fluctuations, till his death on the eighteenth day of observation.

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[1] Deutsches Archiv f. klin. Med. Bd. XIV. S. 242.

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Day of observation.	I. Amount of nitrogen introduced in the food. Grm.	II. Amount of nitrogen excreted in fæces, sputa, urine. Grm.	III. Difference between (I.) and (II.) or amount of deficit. Grm.	Body-weight. Kilogrm.
1	3.12	13.58	10.46	58.330
2	2.44	10.92	8.48	57.891
3	3.36	13.48	10.12	58.217
4	8.18	19.12	10.94	57.730
5	9.13	20.07	10.94	56.870
6	11.96	21.18	9.22	56.055
7	9.02	18.69	9.67	55.030
8	1.20	16.25	15.05	54.877
9	1.20	15.32	14.12	54.735
10	1.21	13.21	12.00	55.935
11	5.94	16.62	10.68	55.270
12	5.30	17.07	11.77	——
13	5.46	18.92	13.46	——
14	6.57	20.71	14.14	——
15	6.57	17.37	10.80	——
16	6.51	25.82	19.31	——
17	6.51	24.51	18.00	——
18	6.35	20.20	13.85	55.960

A comparison of the figures in the three columns headed I., II., III., yields the following results:

1. The quantity of nitrogen given off by the fever-patient (II.) is always greater than the quantity taken in (I.). Hence, the total amount of nitrogen presents a constant deficit, whether there be much or little albumen in the food.

2. The deficit may vary to a considerable extent (III., 8th to 10th day, also 11th to 18th), notwithstanding that the quantity of nitrogen taken in remains approximately constant.

3. An increased supply of nitrogen (I., 2d to 6th day) is attended by relatively trifling fluctuations in the amount of deficit (III.).

4. The lowest values of the deficit (III., 6th to 7th day) coincide with high values of the nitrogen taken in (I.); the highest values of the deficit (III., 16th to 17th, and 8th to 9th days) coincide partly with medium (16th to 17th day), partly with very low values (8th to 9th day) of the nitrogen taken in (I.).

By comparing (2) with (4) we arrive at the following conclusions:

The magnitude of the nitrogen-deficit in fever does not stand in any constant relation to the amount of nitrogen taken into the body. The deficit is not increased by increasing the supply of nitrogen in the food; indeed, the contrary might be asserted with more show of truth.

Inasmuch, therefore, as the consumption of albumen in fever does not appear to be increased by a highly nitrogenized diet, there is no reason for depriving fever-patients of albumen in their food; on the contrary, it seems right that they should have as much of it as their dyspeptic troubles allow them to assimilate.

The question whether albumen may be given to fever-patients thus comes to coincide with the question previously discussed:

whether albuminous food should be allowed in dyspepsia. The propriety of supplying the patient with plastic nutriment, the quantity that may be given, the best form in which to give it, will thus depend mainly upon the degree of dyspepsia associated with the febrile state. Should the fever be intense, the severity of the attendant dyspepsia will render us cautious as to the quantity and quality of the albumen we administer. Should there be a prospect of speedy defervescence, we may even cut off all the albumen for a few days, and keep the patient on fever-diet in the strict sense of the word, *i. e.*, on amyloids and water. But if the fever be prolonged, the necessity for really nourishing the failing patient by giving him albumen grows more urgent from day to day; so that even the most confirmed believers in water-soup (Wassersuppe), gruel, and stale bread, are gradually driven, notwithstanding the continued pyrexia, to resort to yolk of egg beaten up in broth, to milk, and perhaps even to a little roast meat, provided the dyspepsia be not too severe.

Albuminates form an important part, but only a part, of the diet of a healthy man. A mixed diet is also the most suitable for the anæmic. The remarks I made (in the section on Etiology) about the physiological importance of fats, carbo-hydrates, and gelatin, exhibited these substances under a two-fold aspect: first, as richly endowed with potential energy capable of being utilized by the organism for generating heat and muscular contraction; secondly, as limiting the consumption of albumen by undergoing oxidation and dissociation, and thereby contributing to maintain the organic *status quo*. It is obvious that they will be useful in anæmia for the production of heat and the performance of mechanical work. It is equally obvious that a relatively abundant supply of these substances will be stringently indicated in the consumptive forms of anæmia, especially in that associated with hectic fever. They preserve the blood, though they do not help to make it. They are of great service in limiting the degree of the anæmic marasmus, though as regards the actual process of sanguification, they cannot take the place of the albuminates in the dietetic treatment of anæmia. There are certain differences between the three groups of substances in question, viz., fats, carbo-hydrates, and gelatin—differences which may perhaps deserve to be considered in arranging the dietary of anæmic persons. The fats contain the greatest store of potential energy; the carbo-hydrates and gelatin submit most readily to oxidation and dissociation; lastly gelatin, according to Voit, is most effective in preserving the blood and tissues from consumption. Hence it would appear to follow that a liberal allowance of fatty matter should be prescribed when we wish to augment the production of heat and the power of work in anæmic patients; that the carbo-hydrates, on the other hand, and particularly those articles of diet that contain gelatin, are specially indicated when, as in fever, the consumption of albuminates goes on at an excessively rapid rate. As much depends on the actual digestion and assimilation of the food, we ought always to take the relative digestibility of the articles in question into account before we recommend them to our patients. Clinical experience has shown that persons suffering from atonic and other forms of dyspepsia are usually unable to digest much fat; nay, that the products of the spontaneous decomposition of the fatty matters retained in the alimentary canal may actually cause dyspepsia by irritating the mucous membrane. However advantageous, therefore, a liberal supply of fatty matter may appear to be in many cases of anæmia, the quantity given must be proportionate to the patient's digestive powers. This point must never be neglected in ordering fatty articles of diet. Fat is most easily digested when in the form of an emulsion, as in milk. Moreover, the nature of the fatty constituents of milk, and their quantitative proportions, are also important; for we know by experience that food prepared with good fresh butter is not only more palatable, but, upon the whole, more digestible than when some of the cheaper substitutes for butter are employed. Milk that has not been skimmed is thus the best kind of fatty food for anæmic persons whose digestion flags. Their roast meat, too, should, if possible, be basted with good fresh butter. Lastly, yolk of egg, which is rich in oily ingredients, may be given in some suitable vehicle, such as broth or wine. As regards the carbo-hydrates — water-gruel, barley-water, furmity, groat-pap, toast, etc.—I may remark that they are all easily assimilated, and are therefore pre-eminently adapted for sick people whose dyspepsia is extreme, and who are temporarily debarred from albuminates and fats. For the same reason, they are to be preferred in diseases that run a rapid course with high fever, and constitute the chief or only element in "fever-diet," strictly so-called. I have already pointed out that a diet of this sort is only allowable in the more intense forms of febrile dyspepsia, and in fevers which may be expected to run a very rapid course; whereas in fevers of a protracted kind, plastic material in some readily assimilable form must also be provided. In any case, a diet containing carbo-hydrates is preferable to the "diète absolue," *i. e.*, simple starvation; since the introduction of readily oxidizable non-nitrogenous compounds into the blood must lessen the consumption of the albuminous tissues. Their continued and free administration may therefore be counselled, not merely in fevers, but whenever we desire to economize the albumen of the body. To illustrate my meaning, let me refer to the class of weakly people of anæmic-irritable constitution (p. 307); their general health and nutrition may be greatly improved by combining a liberal supply of digestible farinaceous food with a suitable proportion of plastic material, or by sending them to Meran or Montreux for the grape-cure. Those anæmic persons, on the other hand, who are of sluggish temperament, who, notwithstanding their pale complexion and ill-developed muscles, show a disposition to grow fat, should be advised to limit their consumption of fats and carbo-hydrates. Their anæmia gets most benefit from albuminous food; for it is due, not so much to excessive consumption of the blood constituents, as to insufficient sanguification. Moreover, a liberal use of fats and carbo-hydrates would promote the existing inclination to obesity. I need say no more on this subject at present, especially as the indications for including those substances in a patient's dietary may be easily gathered from their physiological significance.

As Voit has proved that the decomposition of albumen in the system may be more effectually restricted by giving gelatin than by giving fats and carbo-hydrates, it is plain that gelatin ought, on theoretical grounds, to be prescribed in the consumptive forms of anæmia, especially in that associated with fever. Senator has recently insisted on the value of gelatin as a constituent of fever diet; he has restored this substance to its proper place among the resources at the disposal of the physician. There is yet another reason why articles of food containing gelatin should be largely used in the diet of fever-patients: they admit of being prepared in a very digestible and palatable form. Bone-broth is rich in gelatin; its flavor may be improved by adding a little Liebig's extract. Clear jellies made of calves'-feet, hart's-horn shavings, isinglass, or French gelatin are excellent when flavored with red or white wine, or with beef-tea or extract of meat. These jellies are a very good way of administering gelatin in cases of febrile anæmia and wasting; their strong and yet cooling flavor is peculiarly grateful to patients suffering from fever, and they serve as vehicles for alcohol and meat-extracts.

The therapeutic value of alcohol is closely connected with that of the class of foods we have just been considering. Alcohol is an important ingredient in the dietary of anæmic patients. We know that it is able to retard the chemical changes taking place in the body, and thus to assist in maintaining the organic *status quo*. It ought, therefore, to be given in extreme anæmia and marasmus from whatever cause, especially if they belong to the consumptive group. But we must not forget that alcohol, besides being an intoxicant, exerts a deleterious influence on digestion; this is manifest after large quantities of wine and beer, and still more after excessive indulgence in more highly concentrated liquors; hence, we must always be cautious in adding alcohol to a patient's diet. Alcohol is most likely to cause dyspepsia in those unaccustomed to its use; when taken habitually, in moderate quantities, it becomes an indispensable stimulus, without which the digestive organs act sluggishly. In many forms of anæmia alcohol is contraindicated, either because we are afraid that it may aggravate the primary disease (as in the symptomatic anæmia due to inflammatory nephritis with albuminuria), or because some complication of the anæmia, such as a tendency to corpulence, renders its liberal consumption unadvisable. While taking all these accessory and accidental circumstances into account, however, we may still affirm that a methodical use of alcoholic beverages, suitably chosen, is of great value in the fulfilment of the *indicatio morbi;* and that, in the vast majority of cases of anæmia, it is not the use but the abuse of alcohol that deserves censure. Wine takes the first place among alcoholic drinks, not only on account of its agreeable taste, but as a tonic. It should be preferred to all its congeners in the treatment of anæmia. No general rules can be laid down about the quantity to be taken daily, or the magnitude of the individual dose. It may be stated broadly that the more habituated the patient has previously been to its use, the larger may be the individual dose; the more extreme the anæmia and debility, the more often may this dose be repeated. The physician should be enough of a connoisseur to decide on the quality of the wine he recommends; he must never allow his patients to injure their health by swallowing trash. Freedom from adulteration is the first requisite; notwithstanding all the theoretical objections of chemists, only pure wine is beneficial; the various artificial compounds which usurp its name, though agreeable to the unpractised palate, exact retribution on the head and stomach. Bordeaux, the more generous wines of Hungary (not too sweet), and Madeira are the best vintages for anæmic patients; they are least prone to cause dyspepsia (when pure), even when the digestive powers are feeble. Unadulterated beer, not too much hopped, and matured by keeping, may be recommended for anæmic women and children; men used to beer may be allowed to go on with it when they are anæmic and want strengthening. Beer contains a considerable proportion of carbo-hydrates (malt-sugar, dextrin); hence, it is not well suited for those anæmic persons who are disposed to corpulence. I need hardly say that alcoholic drinks are not heating in the sense of raising the temperature of the body; indeed, the well-known experiments of Bouvier and Binz have shown that alcohol actually lowers the temperature. Fever, accordingly, does not contraindicate the use of spirituous liquors, especially strong wine; on the contrary, they are doubly beneficial in the febrile forms of anæmia. When fever runs very high, and there is rapid wasting, it is often right to give alcohol in a still more concentrated form, in order to resist, as much as possible, the progress of consumptive change. But the stronger stimulants are very apt to cause dyspepsia; they should, therefore, be selected with great care, and their effects on the digestion closely watched. My own experience is in favor of old Cognac brandy as least likely to upset digestion; hence, I prefer it to rum, whiskey, etc., in the treatment of fever-patients. I give it pure, or diluted with a little water, or rubbed up with yolk of egg and sugar, in doses of a teaspoonful several times a day; at the same time, I am not chary of wine and suitable nourishment.

As I have already had occasion to remark, the dietetic treatment of anæmia chiefly consists in providing the patient with appropriate nourishment. In reference to this point, the physician cannot be too particular or too careful to individualize. But our dietetic measures are not exhausted when we have undertaken to watch and regulate the feeding of our patients; we have also to arrange and control their mode of life (δίαιτα). No universal rules, which shall be applicable to anæmia in all its forms and degrees, can be laid down; different cases may require very different management. The following points deserve attention:

In severe anæmia, whatever its origin, our main object is to lessen, as far as possible, the expenditure of matter and of energy. Hence we prescribe rest for the patient's body, especially rest in bed. Even when the anæmia is less severe, the patient ought to be kept in bed if there be any fever, for the waste due to fever is decidedly increased by bodily movement and exertion. Should it be decided that the patient is to keep his bed for any length of time, an appropriate sick-room must be chosen. When circumstances admit of it, the patient ought to be put into a large, airy room, with plenty of sunlight, and a uniform temperature. We must always bear in mind that want of fresh air and light, and extremes of heat and cold, are among the causes of anæmia, from which the patient requires to be protected as much as possible; otherwise, the beneficial effects of his incarceration are likely to turn out illusory. How long he is to remain in bed will depend (apart from the presence of fever) upon his strength. We must never be in a hurry to let him get up before the fever has wholly subsided, and the anæmic symptoms show decided signs of amendment. He should at first get up for only a few hours daily. Permission to go out of doors must depend on climate, season, and the state of the weather. It may be broadly stated that the air itself can never be otherwise than beneficial in anæmia; hence bed-ridden patients ought always, if possible, to spend the day out of doors (on open terraces, under an awning, etc.). But it must not be forgotten that anæmic persons are very liable indeed to take cold (p. 409); great caution should, therefore, be exercised in permitting them to leave the house when the weather is chilly and variable.

At a more advanced period of convalescence, or when the anæmia is mild from the beginning, should there be no fever, and should the history of the case point less to increased consumption than to defective sanguification as the cause of the anæmic state—under such circumstances, confinement to bed will be as prejudicial as it was desirable under the conditions previously enumerated. The patient ought, if possible, to spend some part of every day in the open air, and need not scruple to take exercise. For the full enjoyment of these advantages, a temporary change of residence is desirable, and may be indispensable. As the patient cannot spend much of his time out of doors in rough and uncertain weather, he must pass the winter months in a milder and more temperate climate. Hence wintering in the South may be advised as a remedial no less than as a prophylactic measure (p. 430), when we desire fully to utilize the roborant effects of open-air exercise during the inclement season of the year. Anæmic persons should also be advised to spend the hot summer months in the cooler forest and mountain regions. This course is specially adapted to remove the lingering traces of anæmia left by severe illness. In a region free from the heat of the plains and the stifling atmosphere of cities, the patient is able to spend a great part of his day in taking open-air exercise, even in July and August, without dangerous or unpleasant consequences. The question of exercise deserves to be further considered. When the patient seeks pure air amid scenes of natural beauty, he is often tempted, before he has fully regained his strength, to over-exert himself prematurely. Beneficial as a moderate, a gradually increasing amount of muscular exercise undoubtedly is to the anæmic convalescent, any single act of imprudence (too long a walk, a mountain tour) is very likely to throw him back and delay his progress to recovery. The patient should always be warned against over-estimating his powers, and forbidden to undertake any distant expeditions for some length of time. Again, he must not be allowed to sit up late; the body is soon tired, and requires long rest in bed and sufficient sleep for its functional and nutritive renewal. So long as any symptoms of anæmia remain, the patient should avoid theatres, balls, and concerts (of which there is never any lack at the more fashionable health resorts). In critical cases, a locality may be selected where the needful modicum of comfort may be combined with a "country life" in the proper sense of the word. Sexual excesses, to which anæmic convalescents are often prone, are obviously hurtful. It is equally clear that pregnancy, in itself a cause of anæmia, is not likely to promote recovery from anæmia otherwise brought on. Finally, the dietetic management of anæmic patients includes attention to their psychical life. Debilitated persons, especially those convalescent from severe disease, ought never to undertake severe mental labor, or return prematurely to their former intellectual pursuits. The energy and quickness of the mental powers are usually inferior to those of volition, and the consciousness of the disproportion between the will and the power to execute causes an uncomfortable depression of spirits, which, like all depressing emotions, is hostile to recovery. Peace of mind, and, above all, uniform cheerfulness and freedom from anxiety, are important elements in the dietetic management of anæmic persons. The physician, and, still more, the patient's relatives and friends, should endeavor to furnish or to preserve these conditions. The caprices of the patient often render this task a difficult one; still, we ought to persevere until his complete recovery allows us to tell him how insufferably he behaved during his convalescence!

The dietetic treatment of anæmia must be combined, when the disease is at all well marked, with the administration of medicinal remedies. The various medicines employed—so far as they are designed to fulfil the *indicatio morbi*—must operate, like the dietetic measures described above, partly by accelerating sanguification, partly by delaying the consumption of the blood. They are either tonics in the strict sense of the term, *i. e.*, remedies which promote the formation of certain blood constituents, or else substances which are credited with the power of preserving the blood. The chief representative of the former class is iron; the latter comprises certain drugs chemically allied to the fats, carbo-hydrates, and gelatin, which share the preservative virtues which we have already stated these articles of diet to possess.

The use of iron in the treatment of anæmia is far older than the rational explanation of its action. The latter dates from the time when the physiological importance of the metal for the body generally, and especially for the genesis of red blood-corpuscles, was first distinctly recognized. Since that time ferruginous preparations have been prescribed with the immediate purpose of promoting the formation of red corpuscles, and especially of their coloring matter—the hæmoglobin; and in this sense we know that chalybeate remedies are pre-eminently "tonic." Now, although the administration of a substance which, like iron, is an essential constituent of the red corpuscles, in conditions of oligocythæmia (or oligochromæmia), deserves to be called rational, although experience has repeatedly proved that symptoms of oligocythæmia disappear more quickly under the use of iron than without it, still, the pharmacodynamics of the metal are by no means clearly understood, and we are altogether ignorant of the actual behavior of the iron after its absorption into the blood. The fact that the healthy organism gets as much iron as it wants from the food, and the fact that only a small fraction of the iron given medicinally actually penetrates into the blood (the major part of it being eliminated as black sulphide from the bowels), are enough to show what obstacles lie in the way of any satisfactory explanation of the *modus operandi* of the metal. We know that a liberal supply of food containing iron (meat, eggs, etc.) is not of itself sufficient, as might have been expected, to correct the state of the blood in pathological oligocythæmia. We also know that in some forms of oligocythæmia (see section on Treatment of Chlorosis) large doses of iron are of more use than small ones, notwithstanding the fact that a large proportion of the remedy passes through the alimentary canal without being absorbed. Accordingly, notwithstanding all our physiological knowledge concerning the importance of iron as a constituent of hæmoglobin, our employment of this metal in the treatment of disease, and still more, our choice of a particular method of administering it in the different forms of anæmia, are still to a great extent empirical, and on this empirical knowledge we must for the present continue to rely. It teaches us that the preparations of iron do really influence the formation of red corpuscles; that their systematic administration is quickly followed by a return of color to the skin and mucous membranes; that the blood itself, when drawn for examination, gradually assumes a deeper tint and grows richer in colored elements. Accordingly, ferruginous remedies ought always to be conjoined with an appropriate diet in the treatment of anæmia whenever (apart from certain exceptional cases, to be alluded to hereafter) oligocythæmia appears from the symptoms to take a prominent place among the fundamental changes in the blood. Moreover, since it is the oligocythæmia, whether primary or secondary (p. 314), that is the most rebellious to all treatment after the causes of the anæmia have been withdrawn, usually outlasting both the lessened volume of the blood and the hypalbuminosis, it follows that chalybeate medication will be particularly useful in those cases in which, after the *indicatio causalis* has been fully met, the oligocythæmia persists in all but its original intensity. Thus, iron is our sheet-anchor in the treatment of convalescents from severe disease who continue anæmic, though free from all local mischief of a gross kind. The more uncomplicated the anæmia, the more decided the signs of oligocythæmia, the more clearly is the employment of iron indicated, and the more certainly may we reckon on its curative effects. Should the causes of the anæmic state, on the other hand, continue in operation, iron may still be of service as a palliative, and may be urgently needed for this subordinate purpose; but, of course, it cannot be expected to cure the anæmia with the same completeness as in the previous instance. Lastly, there are some forms of anæmia in which the use of ferruginous tonics is positively contraindicated, or in which they ought at any rate to be prescribed with the utmost caution. To understand all these points more thoroughly, it will be necessary to enter on a more detailed analysis of the different cases just referred to, and to describe some of their more characteristic features.

A palliative effect may be looked for from the use of iron when the causes of anæmia are such as interfere with the development of red corpuscles—where oligocythæmia is the primary alteration in the blood. We may take as an instance the anæmia which results from disease of the cytogenic organs. Here the oligocythæmia, though it cannot be got rid of, may frequently be restrained by chalybeates, though, of course, the fulfilment of the *indicatio causalis* will always be the more important object to be held in view. Its importance, indeed, is still more striking in many other forms of anæmia, especially those in which the oligocythæmia is *secondary* to hypalbuminosis, the latter being kept up by noxæ of various kinds. In such cases it will be our first business to get rid of the hypalbuminosis, *sc.*, of its causes, before we can expect any benefit from iron. Moreover, the use of iron is prone to give rise to certain collateral effects which appear to be positively detrimental in cases of this nature, and which must always be taken into consideration by the physician.

These collateral effects are concerned, in the first place, with the digestive apparatus. Clinical experience has shown that, of the various digestive troubles occurring in anæmic patients, one only, viz., simple atonic dyspepsia, is susceptible of being relieved and cured together with the anæmia itself by the use of iron. On the other hand, the different varieties of true dyspepsia, which so often stand in a causal relationship to the anæmia, are usually made worse by ferruginous tonics. Hence the necessity for taking the state of the digestive organs into account before we order iron. Should the patient's tongue be clean and his appetite good; should he be able to digest small quantities of any kind of food, particularly meat, without difficulty, while larger quantities immediately give rise to symptoms of disordered assimilation (weight at epigastrium, retching, meteorism, perhaps diarrhœa)—in a word, to the symptoms of simple oligopepsia, we may boldly prescribe iron in large doses. For in these cases the atony of the digestive functions yields more readily to a free administration of chalybeates than to any other plan of treatment. On the other hand, should the patient's tongue be coated, his appetite impaired or destroyed; should there be a tendency to acid fermentation and pyrosis, even small quantities of albuminous or fatty food being followed by fetid or rancid eructations; should he be constantly complaining of oppression at the pit of the stomach, flatulence, a tendency to jaundice, and especially of irregularity of the bowels, and mucous diarrhœa; under such circumstances we must beware of giving iron till the dyspeptic symptoms have been removed. The state of the urine may also help us to decide as to the desirability of ordering iron in any particular case, for in simple atony of the digestive organs it is usually very pale, clear, and of low specific gravity, while in true dyspepsia it is often highly concentrated and loaded with lithates. Should the signs of dyspepsia, though present, be relatively slight, while at the same time there is extreme oligocythæmia with marked feebleness of digestion, we may venture to try iron, beginning with small doses, and prescribing the metal in some form calculated to influence the dyspepsia (*see* below for the different preparations of iron).

Inasmuch as dyspeptic symptoms are almost always present in febrile anæmia, this alone would be a sufficient objection to the giving of iron in febrile maladies. Experience teaches us, moreover, that the remedy is not well borne in high fever with great dyspepsia. Again, Pokrowsky (*loc. cit.*) has found that iron raises the temperature of the body and increases the elimination of urea. These experimental facts are confirmed by clinical observation; for we know that the premature administration of iron during the period of defervescence, or just after the apyretic state is reached, frequently gives rise to a recrudescence of the febrile symptoms. Accordingly, ferruginous compounds are, upon the whole, contraindicated by the presence of fever. We ought to wait for definitive apyrexia before prescribing them; and even then, it is prudent to begin with small doses of some easily digestible preparation of iron. Nevertheless, in very protracted febrile maladies, when the fever is not high and the dyspepsia is not severe, we may sometimes give iron a trial when the oligocythæmia is extreme, and appears at the moment to expose the patient to greater risk than the attendant fever. But even under these circumstances it is but seldom that we shall find iron of use; in most cases, for the reasons given above, we shall find ourselves compelled, sooner or later, to leave it off again.

Again, iron is contraindicated when hemorrhage is either imminent or actually going on. It is said that the tonic influence of the remedy on the heart, by increasing arterial tension, may provoke extravasation when the vascular walls happen to be frail. On the other hand, we must not forget that the fragility of the vessels is often a result of some defect in the composition of the blood, more especially of oligocythæmia;[1] and from this point of view a tendency to bleeding would rather appear to indicate than to contraindicate the use of iron. The physician is often placed in a dilemma at the bedside with regard to the administration of iron; and it often happens that a decision is impossible until the experiment has been tried in the particular case. It is plain that if, notwithstanding the existence of a hemorrhagic diathesis, we resolve to prescribe iron, we must begin with small doses gradually and cautiously increased. But how are we to decide whether iron is to be given at all? As a general rule, the more intense the anæmia and the more feeble the pulse, the more likely are ferruginous tonics to be serviceable. They are least likely to do harm if the bleeding be spontaneous, *i. e.*, not due to excited action of the heart. But our main reliance must be placed on the results of experiment; if a cautious trial of iron is not followed by an increase of the fatal tendency to bleeding, we may prescribe the remedy more boldly. On the other hand, chalybeate remedies are decidedly contraindicated when the anæmia is associated with cardiac hypertrophy; when the individual outbreaks of hemorrhage may be traced to paroxysms of functional excitement of the heart; finally and chiefly, when the injurious effect of iron in the particular case under observation has been experimentally determined. I do not hesitate to say that the cases of anæmia with hemorrhagic diathesis in which the use of iron is contraindicated by the latter, are far from being as numerous as is often supposed. I am likewise of opinion that many physicians are over-cautious in this matter, and often refuse to give iron in cases where it would do good. Lastly, I may add that in the hospital at Basle iron is constantly prescribed with good effect when the degree of anæmia appears to require it, notwithstanding the presence of a tendency to local or general hemorrhage.

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[1] Consult, in reference to this point, the chapter on "Progressive Pernicious Anæmia" (Special Symptomatology).

I should add, in order to prevent possible misunderstanding, that by the "use of iron" in the foregoing pages, I mean its administration for long periods with a view to obtaining its tonic effects, and not the administration of a single dose of some particular ferruginous preparation, in order to obtain a specific effect independent of its tonic action. Some preparations of iron, especially the perchloride, are often used both outwardly and inwardly as styptics; it is clear that the occasional employment of the remedy for such a purpose as this is wholly different from its continuous administration as a tonic.

The multitude of officinal and non-officinal preparations of iron, and the great variety of chalybeate waters at our disposal, give us a choice of methods for administering iron to which no other drug affords a parallel. In choosing a preparation we must consider, in the first place, whether it is capable of being easily assimilated; for only thus is iron beneficial, its indigestible preparations being more likely to do harm than good. Again, we must ask ourselves if we desire to combine with the tonic effect of iron some subsidiary effect peculiar to one of its preparations or obtained from some other remedy. These considerations will make us select now a simple, now a compound preparation of iron, and the dose to be employed in any individual case will then have to be determined on independent grounds. I shall now enumerate some of the most approved iron preparations, and offer a few suggestions as to the best way of employing them:

Metallic iron, in the form of reduced iron, is of great value when we desire the purely hæmatinic action of the remedy; it is easily digested, and enjoys a well-merited popularity in the treatment of anæmia. Owing to its proneness to become oxidized, it is usually prescribed in pills or bonbons (made with chocolate); the dose may vary, in accordance with the special requirements of the case, from three-quarters of a grain to a grain and a half twice or four times a day. Equally worthy of recommendation are several officinal preparations of ferrous oxide, *e. g.*, ferrous lactate (from one and a half to four and a half grains several times a day in pills, powders, or tablets), or the saccharated carbonate (as much as can be taken on the tip of a knife, several times a day), and others. These and similar simple preparations are chiefly employed in the uncomplicated forms of anæmia (*i. e.*, in the idiopathic form, or in those symptomatic forms which persist after the removal of the primary disease to which they are due). Small doses should be prescribed at first; if we find them agreeing with the patient, larger ones may be ordered without scruple. In their mode of action, the alkaline chalybeate waters stand nearest to the above preparations; they contain ferrous carbonate and carbonate of soda; a course of such water is most beneficial when taken at the spring itself, as an abundance of fresh air, and a complete and appropriate modification of all the patient's habits, are associated with the remedial action of the iron. Patients suffering from simple anæmia, when strong enough to travel, may be sent to Pyrmont, Dryburg, Cudowa, Imnau, Steben, Schwalbach, Spa, Seewen, Fideris, and above all, to St. Moritz, where they can "lay in a supply of hæmoglobin" by drinking the waters, enjoying the air, and a suitable diet. The waters are much less effectual when taken at home—the accessory elements in the treatment cannot be enforced with the same success; moreover, the chalybeate waters are very prone to suffer *in transitu*, owing to oxidation of the ferrous carbonate they hold in solution, which is thus converted into the insoluble hydrated oxide of iron.

Preparations containing iron in combination with phosphoric acid or with potash-salts are also very serviceable in cases of simple anæmia. Foremost among them stands the pyrophosphate of iron and soda (from one and a half to four and a half grains several times a day), and the pyrophosphate of iron water, which may now be procured in all great towns, and of which from half a bottle to a bottle (from ten to twenty fluidounces) may be given daily. These preparations are usually ordered with a view to supplying the system with the phosphoric acid as well as the iron required for the red corpuscles. Blaud's pills are in great repute among practical men, and they deserve all the praise they get; they are warmly recommended by F. von Niemeyer in the treatment of chlorosis; their composition (sulphate of iron, carbonate of potash, of each half an ounce; marshmallow root, thirty grains; gum tragacanth, enough to make one hundred and twenty pills. From two to four pills to be taken three times a day) shows that they combine ferrous carbonate (produced by decomposition in the pill-mass) with a considerable proportion of a potash-salt (potassium sulphate). It is difficult to say with any certainty how much of the efficacy of this preparation in extreme oligocythæmia is due to its digestibility, how much to the simultaneous introduction of potassium (an essential constituent of the red corpuscles) into the system. In any case, the *à priori* grounds for combining potassium with iron are quite as strong as those for giving phosphoric acid with the metal; and repeated trials have convinced me that in Blaud's pills we really have a most valuable and speedy remedy for anæmia. At the Basle Hospital, these pills are now almost exclusively employed when it is desired to cure a high degree of uncomplicated anæmia as quickly and as certainly as possible.

In many complicated forms of the disease we desire something more than the tonic effects of iron. For instance, when the anæmia is causally connected with chronic catarrh of the stomach and intestines (p. 445), we prescribe the alkaline chalybeate waters of Franzensbad, Elster, Kissingen, and Tarasp, so long as the symptoms of dyspepsia are present. Again, when the oligæmia has been brought on by a febrile malady, and the patient is suffering from the prostration incident to defervescence, we give the alcoholic and ethereal tinctures of steel before proceeding to the stronger ferruginous preparations, desiring thereby to achieve an analeptic result. Rademacher's *Tinctura ferri acetatis* (from twenty to sixty drops several times a day) is well adapted for this stage of convalescence; it is assimilated even when the digestive powers are very feeble, and may safely be prescribed when there is a moderate degree of pyrexia. When there is a tendency to hemorrhage, and we nevertheless resolve to give iron (p. 469), its compounds with chlorine are generally chosen, especially the solution of chloride of iron (from two to three drops every three or four hours in a mucilaginous vehicle). Lastly, if we want to promote the absorption of an exudation or the involution of some hypertrophied organ simultaneously with the treatment of an oligæmia, we prescribe the iodide of iron. There is no dearth of iron preparations from which to choose, and though it would be a mistake to look for any very subtle distinctions among them, still it is certainly wiser to obey the usual custom of choosing particular preparations for particular forms of complex anæmia, rather than arbitrarily to set aside tradition.

I have yet to say a few words about several remedies and pharmaceutical preparations whose influence, in conditions of anæmic marasmus, is not so much hæmatinic as conservative, and which are chemically allied to certain kinds of food. Foremost among these is cod-liver oil. This famous remedy, whose beneficial influence upon nutrition is so strikingly shown in many marasmic states (phthisis, etc.), may be regarded, chemically, as an animal fat (oleic glyceride, with glycerides of volatile fatty acids) mixed with biliary constituents. It contains extremely minute traces of iodine and bromine; but these do not contribute to its curative effect; the relatively large proportion of calcium phosphate may possibly be of greater moment. Physiologically, cod-liver oil is so far like the other fats taken as food, that it limits the consumption of the nitrogenous constituents of the body and is capable of supplying the organism with energy by undergoing oxidation. Why then should cod-liver oil be administered as a remedy, notwithstanding its nauseous taste, seeing that its action is similar to that of all fatty matters? First, because clinical experience has proved that it is more readily assimilated than any other kind of fat, whether animal or vegetable. Secondly, because it has been proved experimentally by Naumann (loc. cit.) that cod-liver oil traverses animal membranes more quickly and easily than other oily compounds, this property depending on the presence of an admixture of biliary constituents, and possibly explaining its relatively great digestibility. The same observer has also found that cod-liver oil is more readily oxidized than any other fat. These reasons suffice to explain why it should be chosen as a means of introducing a relatively large amount of fatty matter into the system when the digestive powers are weak, in order that it may be oxidized instead of the albuminous constituents of the body. It follows that the remedial employment of cod-liver oil is peculiarly suited to those forms of anæmia in which a liberal supply of fatty matter, though urgently called for, cannot be allowed, owing to the inadequate secretion of bile and pancreatic fluid. In such cases, cod-liver oil may fitly be substituted for the fatty elements of the food. *A priori* reasoning thus confirms the manifold testimony of experience in suggesting the administration of this remedy whenever well-marked anæmia is associated with over-activity of the chemical changes going on in the system, especially with increased decomposition of albumen. Hence the reputation it has justly acquired as an aid to nutrition in all forms of febrile wasting, and which it also merits in other less definite forms of nutritive irritability. Hence, too, its unsuitability in such forms of anæmia as are associated with a slow rate of molecular metamorphosis, a relaxed constitution, and a pasty habit.

Even in those cases where cod-liver oil would seem to be decidedly indicated, we often find it impossible to prescribe it. Some patients are unable to overcome their repugnance to it by any effort of will; others cannot digest it. The latter difficulty may be anticipated when there is much dyspepsia from gastric catarrh. Symptoms of this disorder (furred tongue, anorexia, etc.) forbid the administration of the oil, for it is likely to intensify them. We ought always to begin by giving the oil in small doses and at rare intervals (about one dessert-spoonful in the course of the day); the dose may be gradually increased to from one to three tablespoonfuls daily, when we have satisfied ourselves of the integrity of the digestive functions. It can never be desirable, under any circumstances, to give more than three tablespoonfuls a day.

To mask the taste of the oil, various artifices may be resorted to. A few drops of rum may be added to each dose, or it may be preceded by a peppermint lozenge, or followed by a mouthful of black coffee. The oil may be included in gelatine capsules, or solidified and wrapped in wafers, etc. For further details, text-books of pharmacy may be consulted.

The malt-extract prepared from Trommer's receipt is designed to fulfil much the same purpose as cod-liver oil, carbo-hydrates (malt-sugar, dextrin) taking the place of fatty matter. The simple (much or little hopped) and the chalybeate form of malt-extract are coming more and more into favor as substitutes for the oil; they are more palatable and more easily digested, and should, therefore, be preferred in the dyspeptic forms of anæmia. During the last few years malt-extract has almost entirely taken the place of cod-liver oil in the treatment of phthisis and other wasting diseases at the Basle hospital, and we have as yet found no reason for returning to the use of the latter remedy. The extract may be given from one to three times a day, in doses varying from a teaspoonful to a tablespoonful, in milk, broth, beer, or wine.

Gelatin need hardly be prescribed as a medicine, as it is capable of being dispensed in a more agreeable form by the cook. It is worthy of note, as Senator points out, that the great Sydenham, two centuries ago, used to prescribe gelatin in combination with carbo-hydrates as a roborant, in the form of his well-known "white decoction" (hart's-horn shavings, bread-crumb, of each half an ounce; water, two pints; boil down to twenty-two fluidounces, and add gum Arabic two drachms, and white sugar half an ounce. A cupful to be taken at a time). But if any physician at the present day, either in pious commemoration of a great luminary of our art, or from conservative feeling, should be tempted to order this decoction to be made up at the chemist's, he will find it necessary to rouse the historic sense of the patient beforehand, to prevent his being nauseated by the insipid sweetness of the mess he is desired to take.

It is sufficiently obvious that none of the remedies hitherto enumerated, whether dietetic or medicinal, whether designed to promote sanguification or to diminish the waste of the constituents of the blood, are capable of fulfilling the *indicatio morbi* in the sense of restoring, at once and completely, the deficient elements of the nutrient fluid in their pristine quantitative relation to one another. The blood, viewed as a functionally-active tissue, when it has been withdrawn from the body in great quantity, undoubtedly admits of being *gradually* restored, either wholly or in part, when the tendencies of the anæmic organism and the conditions of its environment are propitious; but none of the modes of treatment hitherto described can restore it *at once* to its previous state; if such *immediate* restoration be possible at all, it must be effected by the direct introduction of fresh and ready-made blood into the empty vessels. But in many cases of acute oligæmia, when death from loss of blood is imminent, and in some cases of chronic anæmia likewise, an *immediate* supply of functionally-active blood is required; hence, the idea of transplanting blood from a healthy individual (man or animal) must needs have suggested itself sooner or later. The history of transfusion shows how this idea has actually been carried into practice.

A detailed account of transfusion—of the fluctuations in professional opinion concerning its value, of the kind of blood that ought to be used, of the instruments, etc., required—cannot be attempted here. It must be left to works specially devoted to the subject, for I have already much exceeded the limits originally assigned to me. The reader who wishes to become acquainted with the history of transfusion may consult the works of P. Scheel, Blasius, Landois, von Belina-Swiontkowski, Massmann, Asché, Leisrink, and others, referred to in the Bibliography (p. 285); he will there find the needful statistical records, both old and new (with the exception of the cases published since 1873). It will also be impossible for me to give an account of the controversies that have lately been raging on this important subject, and that have not yet subsided. Almost every number of our medical journals contains some notice of a successful or unsuccessful case of transfusion, some article on the theoretical aspect of the operation, some practical suggestion about the manner of performing it; such articles are continually reviving discussion on points which are often of cardinal importance. Some of these points are not yet settled; we must therefore be content with a brief summary of those conclusions which are no longer seriously disputed by anybody, together with a few of those controverted points which appear to admit of a provisional settlement.

It is almost universally admitted, in principle, that transfusion, in conditions of extreme anæmia, is a legitimate resource; nay, that in many cases it is imperatively required. The operation cannot be dismissed from consideration as dangerous and reckless; for it has over and over again been successfully performed, and followed by complete recovery, under circumstances of the most adverse kind. Besides the list of successful cases, however, there is another of a less reassuring description, of cases in which transfusion proved wholly useless or only of momentary usefulness; but this is not enough to deter anybody from repeating the operation in certain forms of anæmia whenever they occur. Again, in severe or hopeless cases, is it not better to resort to even an uncertain remedy than to do nothing? Until very recently, transfusion has always been regarded as a last resource in acute and chronic anæmia; and if there is one thing more than another calculated to surprise us in going through the literature of the subject, it is not the number of failures, but the number of successes that have been achieved under the desperate circumstances for which the operation has been reserved. Again, the number of cases in which death can be ascribed with real or apparent justice to the operation itself is extremely small in comparison with those in which the fatal issue can be traced, with more likelihood, or with absolute certainty, to circumstances of another kind, *i. e.*, to the continued operation of the *causa morbi.*

The most recent observations will be excluded from the following estimate of the value of transfusion as a means of saving life, for the operation is nowadays performed much more frequently than it used to be, and in cases of less severity. By combining the tables given by Belina, Asché, and Leisrink, we get a total of 243 cases in which transfusion was performed for acute or chronic anæmia prior to the year 1873. Of these 243 cases, 114 (46.9 per cent.) terminated in complete recovery; in 34 cases (14 per cent.) the operation was followed by temporary benefit, but failed to save life; in 95 cases (39.1 per cent) no beneficial result whatever was achieved. Accordingly, transfusion has failed in a little over a third of all the cases published before 1873, while in nearly two-thirds of the total number it has been followed by improvement or recovery. These figures would suffice, as they stand, to justify the operation, even if we did not know that it had almost invariably been resorted to in desperate cases. If we examine more closely into the details of each failure, we find that in a vast majority of them death cannot be ascribed directly or indirectly to the operation, but was due to other causes. An accurate sifting of these causes, however, is impracticable; for the estimate of the probable duration of the patient's life in each case, supposing transfusion not to have been performed, would be too much at the mercy of the individual judgment of the critic. I may therefore leave the reader to consult the original records for himself, and arrive at an independent opinion on the subject.

It is not difficult to show that transfusion is a legitimate operation. Neither is there any difficulty in deciding what are the cases of anæmia in which it may be undertaken with the best prospect of success. A favorable result may be anticipated from a timely recourse to transfusion whenever acute oligæmia is brought on by loss of blood in a previously healthy person. Acute anæmia, after post-partum hemorrhage, offers the best chances of success; always supposing the actual bleeding to have been brought under control, and no fresh outburst to occur. Apart from the latter accident, it is in such cases that the greatest number of successes has been hitherto achieved.

In 113 of the 243 cases alluded to above, the operation was performed on account of hemorrhage during or immediately after delivery. Of these 113 cases 67 ended in complete recovery, 7 showed only a temporary improvement, while 39 terminated fatally, without any sign of previous amendment. A positive result was thus achieved in 65.5 per cent., or two-thirds of all the cases belonging to this category; of this proportion, moreover, 59.3 per cent. were recoveries, while in only 6.2 per cent. was the improvement temporary. As the recoveries amount to more than half of the total number of cases, the obstetrician must consider transfusion obligatory whenever acute anæmia of sufficient severity to threaten life sets in as a result of hemorrhage during delivery—the hemorrhage itself having been arrested. The relatively favorable prognosis of the operation, when performed in connection with the puerperal state, must be attributed chiefly to the extraordinary power of bearing loss of blood, with which the female sex—particularly at this critical period—is endowed (cf. p. 420).

The results of transfusion in cases of acute anæmia following wounds and surgical operations, though less brilliant, are nevertheless encouraging. The chances of complete recovery (not of temporary improvement) are least promising in acute anæmia from internal disease, and in chronic anæmia. As regards the latter, indeed, future statistics are likely to be more favorable than those of the past. Of late years, transfusion has been resorted to earlier, and not as a last and desperate measure; and its early performance seems to hold out better prospects of success in the chronic forms of anæmia.

In 46 of the 243 cases alluded to above, acute anæmia had been produced by wounds and surgical operations. In 19 cases transfusion was followed by complete recovery; in 7, by temporary improvement; in 20, by no result at all. The percentage of complete recoveries thus amounts to 41.5 per cent.; of cases temporarily benefited, to 15.2 per cent.; of failures, to 43.5 per cent. The residue of 84 cases is made up of acute and chronic forms of anæmia associated with visceral disease. Of this number 25 terminated in complete recovery; 25 received temporary benefit; in 34 the operation failed to do any good. (Percentage ratios: 29.8, 29.8, and 40.4.)

The general conclusion to be drawn from the figures I have given (which do not include the more recent cases of transfusion, performed with a better knowledge of the indications, and therefore with better results) is that the number of cases cured and temporarily benefited, taken jointly, exceeds the number of failures in all categories alike—though not, of course, in the same ratio. Hence, transfusion may be confidently recommended in extreme anæmia: first, when there is immediate danger to life; secondly, when all hope of a favorable issue is not nullified by the malignity or the undiminished obstinacy of the causes of the anæmic state.

Both of the above indications are more often found associated with acute than with chronic anæmia. For in the former class of cases the immediate danger, and therefore the necessity for immediate interference, are much greater than in the latter.

Again, the causes of chronic oligæmia are not usually capable of being instantaneously removed, or even moderated. Those cases of acute anæmia are best suited for treatment by transfusion in which the causal hemorrhage is within reach of styptic measures. Hence, it is chiefly to obstetrical practitioners and surgeons that we must look for any large experience of the operation; though a more extensive employment of transfusion in visceral diseases may fairly be anticipated likewise.

There is not much difference of opinion at the present day concerning the principles I have just laid down. There is much less unanimity concerning the mode in which transfusion may be most suitably and least dangerously performed. The first question refers to the choice of blood, to the "physiological technique" of transfusion (Juergensen). But this question, when looked at more closely, branches out into two others: first, whether human blood or that of the lower animals should be employed; secondly, whether the blood ought or ought not to be defibrinated.

There can be no doubt that direct transfusion of non-defibrinated human blood from a healthy subject is the best, because the most natural method. It is equally certain, however, that the rapidity with which human blood coagulates (in less than five minutes) forms a very serious obstacle to its employment. Nevertheless, it has been repeatedly employed of late years without any special precautions against the occurrence of coagulation (Rautenberg, Braxton Hicks, Carey, Savage, and others), though the risk of embolism must always make the proceeding a very rash one. Many attempts have been made to obviate this risk by adding various salts to prevent coagulation (Neudoerffer, Braxton Hicks, Richardson, and others), or by employing ingenious though complicated instruments (Gesellius) for transferring the blood of the giver to the vessels of the receiver with as little delay as possible. For my own part, however, I agree with Juergensen, Leisrink, and many others, in thinking that no really simple, safe, and universally applicable method of transfusing unaltered human blood from one individual to another has yet been contrived.

But is there any urgent necessity for such a contrivance? Is not defibrinated human blood quite as effectual for the end in view as non-defibrinated blood? Has it not hitherto been almost invariably employed, and often with the best results? The objection that valuable time may be lost in defibrinating the blood may possibly apply in certain cases, where the physician has to work single-handed; otherwise, the exposure of a vein in the patient, putting a ligature round it, and introducing a canula, must occupy more time than opening a vein in the giver and whipping the blood, when simultaneously performed by an assistant. The paradoxical notion that venous blood, which has become bright red by being agitated with air, does not owe its change of color to the same cause (oxygenation of hæmoglobin) as that which converts venous into arterial blood in the pulmonary capillaries—that the blood is actually deprived of the needful "vitalizing power" (Gesellius), is hardly worthy of serious discussion. But there is another objection that seems at first sight to be more plausible: the removal of the fibrin—of one of its essential constituents, may be supposed to deprive the blood of its vitality. Gesellius says, with vigorous emphasis, that the blood is "whipped to death." But what is the supreme importance of fibrin (or, more correctly, of fibrinogen), that its removal should be denounced so vehemently? This we are not told; indeed, in the present state of our physiological knowledge, it would be impossible to tell. There is not the slightest ground for supposing that the introduction of defibrinated blood may cause serous or sanguinolent transudation into the lungs or the intestines (as was rather prematurely affirmed by Magendie on the strength of a single experiment), or that fibrinogen plays any active part in the nutritive and respiratory processes. On the other hand, it has been established, by a number of trustworthy observations and experiments, that both in man and in the lower animals, defibrinated blood obtained from the same species is fully equivalent in its essential physiological properties (whether nutrient or vitalizing) to blood which has not been deprived of its fibrin (Prévost and Dumas, Dieffenbach, J. Mueller, Bischoff, Brown-Séquard, Panum, Landois, Ponfick, et al.). Accordingly, so long as we have no satisfactory means of transfusing non-defibrinated human blood without the risk of coagulation and embolism, we must unhesitatingly use defibrinated blood, supposing human blood to be obtainable at all; and human blood is to be had more frequently than the advocates of transfusion from the lower animals are inclined to admit. It is certainly untrue to assert, in general terms, that blood is more easily to be procured in cases of emergency from the lower animals than from the human subject. The exact contrary would be more near the truth. Does any one suppose that lambs and calves are to be had at a moment's notice, ready to yield the necessary blood? It is far easier, when a life is trembling in the balance, to find some man who, either for love or money, will give of his superfluity to a fellow-creature in urgent peril. Away, then, with all superfluous pessimism!

The problem takes a different form when the blood of an animal happens, accidentally, to be more easily procurable than human blood, or when we can choose between the two. We must decide, first, whether transfusion from one species to another is allowable under any circumstances; secondly, granting that it is allowable, whether the blood of one of the lower animals is to be preferred to defibrinated human blood for the purpose.

A final settlement of these two questions happens to be peculiarly difficult at the present time. Moreover, the writer of a text-book is bound to be specially prudent in deciding between conflicting opinions. Notwithstanding isolated instances of the successful transfusion of blood from lower animals, published both by old and by recent writers (Lower, J. Denis, Bliedung)—instances quite worthy of credit—it has been generally believed by physicians and physiologists, ever since the well-known experiments of Prévost and Dumas (1821), and the still wider investigations of Panum, that blood from an animal belonging to another species exerts a hurtful—nay, a poisonous influence, and that transfusion can only be performed with success, whether in man or in the lower animals, when the blood employed is drawn from an individual of the same species (dog's blood for the dog, human blood for man). Such was the accepted doctrine for many years. In our own day, however, transfusion of blood from the lower animals to the human subject has again found enthusiastic advocates (Mittler, Gesellius, Rautenberg, O. Hasse, and others). They bring forward a series of favorable, occasionally very brilliant results, and warmly urge the superiority of the direct transfusion of non-defibrinated lamb's blood over that of defibrinated human blood. Within the last twelve months, since the appearance of O. Hasse's very striking paper, in which he gives the results of the first fifteen cases (mostly favorable), in which he transfused lamb's blood into the vessels of the human subject, the number of such attempts has been on the increase. These attempts have not all been crowned with success; still, we have learned from them that the belief in the injurious properties of blood derived from another species can no longer be held in its previous absolute form, and requires qualification. In this way one of the most important and fundamental principles relative to transfusion has once more been shaken, and, as we shall see immediately, the reopened question has not yet received a definitive answer. I must, therefore, content myself with a rough sketch of the shape which, as I believe, that answer will ultimately take.

Hasse's earliest communications were enough to show that direct transfusion of moderate quantities of arterial blood from the carotid of a lamb into the veins of the human subject might exert a decidedly beneficial influence upon the constitutional symptoms in various forms of anæmia and marasmus. The roborant effects of this operation were repeatedly manifested, not only in cases of acute anæmia, but also in the chronic anæmia of phthisis and other exhausting diseases. Hasse did not scruple to recommend his method as being both effectual and free from danger. Nevertheless, his own statements have made us acquainted with a series of pathological changes and peculiar symptoms more or less invariably consequent upon the transfusion of blood from an animal of another species, and quite unknown after the transfusion of defibrinated human blood. It is not till after the patient has run the gauntlet of these dangers that he begins to feel the benefit of the operation. A feeling of imminent suffocation and actual syncope were frequently observed when the blood was allowed to flow into the veins too rapidly and for too long a time; but these are symptoms which have been noticed after the incautious introduction of large quantities of defibrinated human blood. The symptoms I am now about to mention are, however, of a more peculiar kind. Rigors, severe though brief, attended by a great rise of temperature, have been observed both by Hasse himself and by all his imitators. These rigors almost always occur during the twenty-four hours immediately succeeding the operation. Again, peculiar disturbances are not unfrequently developed in the kidneys; partial suppression of urine and hæmaturia being their most important symptoms, from a clinical point of view (O. Hasse, Sander, Thurn, Klingelhoefer, Bruegelmann, and others). Concerning some other less usual phenomena (extensive thrombosis in the vein employed for transfusion, phlebitis, etc.), I will say nothing; for although their occurrence may possibly be connected with the transfusion of dissimilar blood, that connection is not susceptible of being proved. I will also pass over the risk of coagulation of the blood *in transitu*, a risk not wholly obviated by the procedure of Hasse and Gesellius; for it is due to the blood not having been previously defibrinated, and it is obviously independent of its having been derived from an animal of another species.

The cause of the peculiar and violent febrile paroxysms (Hasse himself has seen the temperature rise to 42° C. = 107.6° F.) is still obscure, but the phenomenon, though usually of short duration, ought to make us hesitate before we recommend the transfusion of lamb's blood for general adoption. The hæmaturia and associated disturbance of the renal functions have, however, been fully elucidated by the laborious researches of Ponfick. Not only do his experiments endow the renal symptoms in question with a wider range of clinical significance than they seem at first sight to possess, but they further contribute, n a very desirable way, to the solution of the two fundamental problems with which we are at present concerned.

Ponfick ascertained that in dogs, rabbits, etc., neither hæmaturia nor any other grave symptom was produced by the careful njection of small or considerable quantities of blood, defibrinated or not defibrinated, taken from an animal of the *same* spe-ies, while relatively small quantities of blood from an animal of a *different* species always sufficed to cause severe hæmaturia. When the quantity of dissimilar blood tranfused was considerable, the operation was invariably followed—no matter whether the blood had been previously deprived of its fibrin or not—by almost absolute anuria, speedily terminating in coma and death (within from 36 to 48 hours).

Ponfick's experiments were conducted on a large number of animals belonging to widely different species, but the results obtained were always the same. Thus, for instance, hæmaturia or suppression of urine occurred in the dog, whether human blood, or that of the cat, lamb, calf, pig, rabbit, hen, or duck, was employed for transfusion. Similar effects were produced in the rabbit and the cat by injecting blood from other animals into their veins. The minimum dose of alien blood required to produce hæmaturia was found to vary considerably in amount, the variations being constant for any two species of animals. These interesting relations may be gathered from the following table. The right hand column of figures represents the percentage ratio of the defibrinated alien blood destined for transfusion, to the body-weight of the animal subjected to the operation:

I. *Dog.*

	Limit of Hæmaturia after indirect transfusion of:
Blood of cat	from 0.36 to 0.40 per cent. of body-weight.
" lamb	" 0.12 to 0.13 " " "
" calf	" 0.14 to 0.16 " " "
" pig	" 0.13 to 0.15 " " "
" rabbit	" 0.23 to 0.25 " " "
" man	" 0.12 to 0.13 " " "
" fowl	" 0.43 to 0.45 " " "

II. *Cat.*

Blood of dog	less than 0.4 per cent. of body-weight.
" lamb	from 0.20 to 0.30 " " "

III. *Rabbit.*

Blood of dog	from 0.05 to 0.10 per cent. of body-weight.
" lamb	" 0.05 to 0.10 " " "
" pig	more than 0.05 " " "
" fowl	from 0.10 to 0.20 " " "

Another very curious fact becomes apparent on consideration of the above figures, viz., that the magnitude of the minimum dose is entirely independent of the mutual relation between the two animals in the zoölogical scale. Lamb's blood begins to cause hæmaturia in the dog when it reaches 0.13 per cent. of its body-weight, while that of the fowl does not begin to do so till it reaches 0.45 per cent. The blood of the cat and that of the fowl are nearly on a par as regards their power of causing hæmaturia in the dog (0.40 per cent., 0.45 per cent.). The minimum lethal dose varies with the minimum dose required to produce hæmaturia. Thus, Ponfick ascertained that lamb's blood (whether transfused directly or indirectly) proves fatal to the dog in doses of from 1 to 1.2 per cent. of its body-weight, while fowl's blood did not cause death till the dose reached 2 to 2.5 per cent. On the other hand, dog's blood (blood from the same species) was injected in enormous doses into dogs (6.4 per cent. of the body-weight) without producing any ill effect, no trace even of hæmaturia having been detected when the transfusion was carefully performed.

The probable cause of death after transfusion of alien blood, and the essential character of the hæmaturia, are both satisfactorily elucidated by Ponfick's experiments. Peculiar alterations in the kidneys are invariably found both in animals who succumb to the operation, and in those, less seriously affected, who are killed for purposes of examination. Both kidneys are always greatly swollen; large portions of the straight and convoluted tubuli are found blocked up by granular and blood-stained casts, a variable number of which may be detected in the scanty and sanguinolent urine. These appearances are sufficient to account for death; and, taken together with the symptoms presented during life, they entitle us to conclude with a high degree of probability that any considerable quantity of alien blood introduced into the circulation sets up an acute nephritis which tends, when at all severe, to a rapidly fatal issue with uræmic symp-oms and suppression of urine.

But what is the immediate cause of this peculiar, often so angerous nephritis? Ponfick's experiments furnish an answer o this question too; moreover, they throw an unexpected light n the true nature of the hæmaturia. Inspection with the naked ye, and still more conclusively, microscopical and spectroscopic xamination, show that the red color of the urine is not due to he presence of red corpuscles, but to that of large quantities of issolved hæmoglobin. Strictly speaking, therefore, we have to do not with a hæmaturia, but with a hæmoglobinuria; and as the coloring matter may also be demonstrated both in the ocular media and in the fresh plasma of the animal subjected to the operation, no doubt remains as to the cause of the interesting phenomenon in question. It is clear that the mingling of two dissimilar kinds of blood is followed by a profound alteration in the mingled fluids—an alteration consisting in the removal of the coloring matter from an immense number of red disks, and a consequent annihilation of their functional vitality. By repeatedly examining blood, taken from the animals operated on, under the microscope, Ponfick has convinced himself that it is not the corpuscles proper to the animal, but those newly introduced into its circulation, that lose their coloring matter and are converted into "spectres." Further, the plasma holding the hæmoglobin in solution acts as an inflammatory irritant upon those organs which are chiefly entrusted with the dangerous task of eliminating the alien element from the system. The passage of the hæmoglobin through the kidneys is attended, in virtue of the phlogogenic properties of this substance, by the above-described nephritis, which may occasionally, as I have already pointed out, prove fatal. That it is really the hæmoglobin which exerts this deleterious influence on the renal parenchyma is proved, according to Ponfick, by the fact that blood, even when derived from an animal of the same species, acquires phlogogenic properties when allowed to give up its coloring matter to the plasma [to become "laky"] before it is employed for transfusion.

That it is not the corpuscles proper to the animal, but those introduced by transfusion, which yield up their coloring matter to the plasma, was conclusively proved by microscopical examination of the blood in cases where the autochthonous and the alien corpuscles differed widely in form and size, *e. g.*, where fowl's blood was infused into the veins of the dog. The following experiment proves that the hæmoglobinuria is the connecting link between the presence of hæmoglobin in the plasma on the one hand, and the consecutive nephritis on the other: blood drawn from a dog was rendered "laky" by freezing, according to Rollett's well-known method; and this blood was found to produce exactly the same poisonous effects upon another dog as were produced by the transfusion of alien blood derived from the fowl. That hæmoglobinuria in the human subject, whatever its cause, may also be associated with symptoms of violent nephritis, is proved by many recorded cases in which a fatal attack of acute nephritis was observed to occur in immediate connection with a true hæmoglobinuria of unknown origin. I have myself published, under the name of "hæmatogenic icterus," a very interesting case of this sort which occurred in the Basle hospital, but in which, of course, the causal bond between the hæmoglobinuria and the nephritis was not recognized at the time (*Deutsch. Archiv für klin. Med.* Bd. XII. S. 502).

I have been obliged to go rather deeply into these complicated matters in order to arrive at a provisional settlement of the two questions formulated above. Those questions were: (1) Is it allowable, under any circumstances, to transfuse blood from one of the lower animals into the human subject? (2) Is the direct transfusion of non-defibrinated blood from one of the lower animals to be preferred to the indirect transfusion of defibrinated human blood? I have pointed out that the most recent results of experimental inquiry (confirming the belief in the poisonous properties of alien blood and elucidating the true nature of its action) are at variance with the clinical achievements of O. Hasse and others in transfusing blood from the lamb to the human subject. But the positively remedial effects of lamb's blood are only obtained, as may be seen from the clinical records themselves, after the patient has weathered a perfect storm of grave symptoms, closely resembling those produced by the injection of alien blood in the experiments of Prévost and Dumas, Panum, Ponfick, and others. The ominous presence of hæmaturia, or rather hæmoglobinuria, confirms the analogy between the experiments performed on animals and the clinical observations made on the human subject. We cannot but conclude that the transfusion of any considerable quantity of lamb's blood is a risky procedure, which may, indeed, ultimately cure the patient, but which may also kill him by setting up serious mischief in his kidneys. Sander lays the needful stress on this objection to the transfusion of lamb's blood; he recommends the employment of such blood only when no other can be got, and insists that it must always be injected in small quantities. Again, as we have no means of knowing beforehand what the effect of other kinds of alien blood upon the human body may turn out to be, while we do know from experience that the blood of the lamb, and perhaps that of the calf also, is comparatively innocuous, we shall do well to be guided by this knowledge and to abstain from clinical trials of blood drawn from the dog, pig, etc. The following, then, is the answer which we may fairly give in the existing state of our knowledge, to the question whether the transfusion of blood from one of the lower animals to man is allowable: "The transfusion of small quantities of blood from the lamb to the human subject may, under certain conditions, be legitimate, but the transfusion of any considerable quantity of it is always dangerous."

But what prospect of advantage can there be from the transfusion of alien blood, seeing that its red corpuscles are, in all likelihood, dissolved or robbed of their coloring matter in the human circulation? The "hæmaturia" noticed to occur in man after transfusion of lamb's blood seems to leave no doubt on this point; and, although the symptom in question was not observed after transfusion of smaller quantities of lamb's blood, still we must recollect that, in Ponfick's experiments, hæmoglobinuria was only produced after a certain minimum of alien blood had been exceeded (p. 484). It is clear that in no case can the absence of hæmoglobinuria be taken to prove that the red corpuscles of the alien blood survive their transplantation; moreover, this is confirmed by another of Ponfick's experiments. He found that hæmoglobinuria was absent after the injection of small quantities of "laky" blood derived from the same species, and only made its appearance when the injection was repeated, or when the original dose was a large one. It is evident that small quantities of free hæmoglobin are susceptible of being oxidized in the system and in this way got rid of, so that the absence of hæmoglobinuria in man after the transfusion of small quantities of lamb's blood proves nothing against the proposition that alien corpuscles are speedily destroyed in the human circulation.

When all these facts are duly considered, it will appear, I think, that the favorable effects clinically observed after transfusion of blood from the lamb can only be explained in one of two ways. We must suppose, either that the alien corpuscles are capable of exerting a vitalizing influence (analogous to that of a volatile stimulant) on the organism during its struggle with imminent death, before they are themselves destroyed, or that the beneficial influence of the alien blood is due, not to its corpuscles, but to the albuminates and other constituents of its plasma. Whether the *stimulant* action of lamb's blood is equal to that of defibrinated human blood appears, to say the least, doubtful. On the other hand, the *roborant* effects obtained by Hasse, which induced him to resort again and again to the transfusion of lamb's blood in cases of extreme anæmia and marasmus, may be in some measure explained by reference to the second of the two hypotheses suggested above. Transfusion of lamb's blood would thus take its place among other modes of artificial nutrition; prudently employed, and, if necessary, repeated more than once, it may be deserving of attention as a possible means of supplying a broken-down patient, who refuses food or whose digestive apparatus requires rest, with a certain quantity of nourishment. But might not the fresh serum of lamb's blood be equally efficient for this purpose, without the risk incidental to the transfusion of the blood itself?

Ponfick has shown experimentally that large quantities of the serum of lamb's blood may be injected into the veins of the dog without any ill effect, although the blood itself has a peculiarly hurtful influence upon this animal. This is a point that deserves consideration before we proceed to speculate on the possible good effects of injecting lamb's blood into the veins of the human subject.

A few words about the operation itself. For details, the reader may consult works specially devoted to the subject, and manuals of operative surgery. The utmost care and cleanliness should be observed in dissecting out and opening the vein, which it is not always easy to find in anæmic patients. This little operation may be performed under carbolic or salicylic spray (Thiersch), to obviate all risk of septic contamination. When we resolve to employ defibrinated human blood for transfusion (and this will be in the majority of urgent cases), we should select a vigorous donor, and entrust the duty of drawing, defibrinating, and filtering the blood to an assistant, while we are engaged in preparing a vein for its reception. The blood ought to be kept at a temperature of 37° to 38° C. (98.6° to 100.4° F.). I prefer Hueter's simple transfusion-syringe, which holds 20 c.c. of blood, to all complicated instruments, which are always liable to get out of order at the wrong moment. The blood should be injected towards the heart, slowly, and under a gentle and uniform pressure. No air-bubbles must be allowed to enter the vein. The more slowly the blood is injected, the greater the quantity that may be introduced without causing a feeling of oppression or suffocation; this unpleasant accident is very prone to occur, especially at the outset, when the injection is too rapidly performed. Dyspnœa is always the signal for a pause; the injection must not be recommenced till the breathing has once more become regular and quiet. Worm Mueller's beautiful experiments to show the connection of the arterial blood-pressure with the amount of blood in the vessels, furnish an adequate explanation of the liability to alarming paroxysms of dyspnœa associated with imprudent haste in the performance of transfusion. Such paroxysms hardly ever occur, or only at a later stage, when the blood is slowly and carefully injected. Mueller found that the vascular system, owing probably to some regulative action on the part of the vaso-motor nerves, is capable of rapidly accommodating itself, within very wide limits, to variations in the total volume of the blood, without the occurrence of any marked alteration in tension, or of dilatation of the vessels, or indeed of any pathological phenomena. It is only at the outset, if the volume of blood injected be considerable, that the blood-pressure rises and the heart is called upon to do more work; so that if we take care to inject slowly, allowing the vascular system time to accommodate itself to the increase of its contents, we may prevent undue strain upon the patient's enfeebled heart, and obviate all risk of cardiac paralysis. For there seems to be no doubt that the starting-point of these suffocative paroxysms is the heart, and that they are really due to a momentary failure of its powers.

The total amount of blood to be injected must be determined (apart from the subjective sensations of the recipient) by the state of the pulse. When we find the pulse getting stronger, and the temperature of the peripheral parts of the body more nearly normal, we may advantageously stop. From 100 to 180 c.c. of blood will usually suffice when the anæmia is not extreme, especially in chronic cases, and when we have reason to think that it will be necessary to repeat the operation more than once.

On the other hand, when the anæmia is intense and of acute origin, 200 c.c. or more may be required. I have already said that when the operation is performed slowly and deliberately, the quantity of blood injected may be very large without any risk of a momentary over-distention of the vascular system; hence, it is superfluous, and indeed irrational, to take blood from a vein as a preliminary measure; unless, of course, there be some qualitative abnormality which we desire to correct by the substitution of fresh blood. The after-treatment of the little wound must be conducted on general principles; antiseptic dressings, which ought not to be meddled with till the incision has quite healed, will obviate all risk of septic contamination.

By way of preventing the danger of embolism from the vein, and of the entrance of air into the vessels, Hueter has lately recommended arterial transfusion as originally suggested by A. von Graefe. The blood is pumped into the distal end of a divided artery (the radial or the posterior tibial below the inner malleolus). The first part of the operation consists in denuding the artery, and opening it, with every precaution against loss of blood. The artery is isolated to the extent of two or three centimetres, and four ligatures are passed under it. The proximal ligature is tied, and the afflux of blood from the heart shut off; the distal one is simply looped round the vessel, and tightened so as to arrest the collateral circulation likewise. The artery is then opened, and a canula tied in with one of the intermediate ligatures. The blood is then injected, the looped ligature being relaxed during its flow, and tightened again while the syringe is being refilled. When the operation is completed, the distal ligature is firmly tied, and the isolated portion of the artery between the ligatures removed. The operation is more troublesome than that usually performed for transfusion. The injection sometimes fails, owing to the difficulty of overcoming the resistance offered by the pressure in the peripheral part of the vessel, which is still supplied with blood by collateral anastomoses. Nevertheless, arterial transfusion undoubtedly presents the advantages enumerated above; moreover, it is less likely to be followed by momentary over-distention of the heart. The results hitherto obtained (Hueter, Havemann, Albanese, Koenig, and others) are, upon the whole, encouraging; but the operation has not come into general use.

The above fragmentary survey of the more important points connected with transfusion must suffice, as I am not writing a monograph on the subject. The reader who desires more information may consult the special memoirs and treatises I have referred to. I now pass on to say a few words about the symptomatic treatment of anæmia.

Indicatio Symptomatica.

Although the symptoms of anæmia usually disappear as the blood returns to its normal state, still the physician is often called upon to deal with special symptoms incidental to oligæmia apart from the tonic treatment of the fundamental disease. Particular symptoms may attain an independent gravity, so that the *indicatio vitalis* requires them to be independently opposed; or they may interfere with the fulfilment of the necessary constitutional treatment. The symptomatic measures we are now to consider are as various as the symptoms presented by anæmia, so that a few of the principal ones will have to be selected, to the exclusion of the rest.

Among the constitutional symptoms of anæmia, dropsy occasionally calls for special treatment. It may be caused by the hydræmia incidental to disease of the kidneys, or by hydræmia and hypalbuminosis due to other causes. When the patient's life is directly imperilled by the advancing dropsy, we may be obliged to prescribe hydragogue remedies for the symptom, together with the tonics designed to remove its cause; or a strengthening diet, with iron, may be combined with diaphoretic measures, as recommended and successfully practised by Liebermeister, Ziemssen, Leube, and others; or we may give saline diuretics, among which the acetate of potash, in large doses (from one to four drachms a day), is much employed at the Basle Hospital in the treatment of dropsy. Stimulating diuretics (squill, juniper, etc.) should be avoided when the hydræmia is due to renal disease; and even when it is due to other causes, the adverse influence of these drugs on digestion should make us hesitate before prescribing them. Turning next to the hydragogue plan of treatment, it may be affirmed that drastic purgatives are least suitable when the dropsy is associated with marasmus. By exciting violent peristalsis, they hinder the absorption of nourishment, and promote the inanition of the already enfeebled patient (p. 330). They should only be resorted to in the last instance, after diuretic and diaphoretic remedies have failed.

Inasmuch as anæmic patients (when non-febrile) generate comparatively little heat, and, when much emaciated, part with a great deal by conduction, radiation, and evaporation (owing to the extent of surface presented by their bodies), and are therefore easily chilled, they must be kept warmer than healthy people (warm rooms, clothing, blankets, etc.). Broken-down subjects are so prone to shiver, and complain so much of feeling cold, that we may find it necessary to order hot flannels, hot-water bottles, and hot drinks (coffee, punch, grog), and thus to supply an artificial substitute for the natural warmth in which they are deficient.

Among the local phenomena of anæmia, cardiac weakness and the symptoms of cerebral anæmia are most in need of special treatment. When in a case of acute oligæmia we find the pulse failing, and the heart's impulse growing weaker, till life itself appears to tremble in the balance; or when, in chronic anæmia, temporary over-exertion of the heart is followed by a condition of cardiac paresis, we must boldly administer powerful and quickly-acting stimulants. Foremost among these stands alcohol; whether in the form of champagne, whose stimulant effects are unfortunately as short-lived as they are instantaneous; or in that of the heavier and more fiery wines (Tokay, Madeira, Marsala, Sherry), which are slower and more lasting in their action; or, finally, in that of grog or punch, whose temperature assists their stimulant operation. The dose must be apportioned to the age, sex, and previous habits of the individual; but, when life is in danger, we need not be afraid of slight intoxication, and may give alcohol freely both to women and children. Strong coffee laced with brandy, tea, beef-tea and Liebig's extract, are all excellent; should the last-named article be at hand, a large dose may unhesitatingly be given without previous dilution. Among pharmaceutical agents, camphor is specially worthy of notice; it may be given in powder, or rubbed up with yolk of egg, in doses of from three-quarters of a grain to a grain and a half every hour, or every other hour, until the pulse and cardiac impulse have grown stronger. Musk, too, is often useful, if given in adequate doses (from a grain and a half to three grains every hour), and not reserved till the patient is at his last gasp. Absolute rest is essential, and everything likely to impose superfluous labor on the heart must be scrupulously avoided, *e. g.*, emotional excitement, talking, bodily exertion—especially straining at stool, by which the exhausted patient is often exposed to great risk (p. 346). Constipation should always be obviated by clysters or mild laxatives; under no circumstances ought a patient, confined to bed owing to extreme anæmia, to be allowed to use the night-stool; he should always be provided with a bed-pan while in a recumbent posture. By keeping the patient horizontal, we give his heart less work to do, and prevent the risk of cerebral anæmia as far as possible. Should syncope nevertheless be imminent, even the pillows ought to be withdrawn; if the patient happen to be sitting up or standing, he must instantly be made to lie flat upon the ground. It is quite a mistake to raise a fainting person, as is not unfrequently done by ignorant bystanders, or even by inexperienced doctors, from motives of ill-advised humanity; this usually brings on a fresh fainting-fit. On the other hand, all tight articles of clothing ought to be loosened (neck-tie, collar, etc.), for this removes impediments to the freedom of the circulation. Should the patient nevertheless remain unconscious, and the syncope appear to pass into actual paralysis of the heart, cutaneous irritation (mustard plasters, friction with a flesh-brush, electrical stimulation, etc.) should be substituted for the internal administration of stimulants so long as the patient continues unable to swallow. I might go still more fully into the various methods of resuscitation, but I am afraid of exhausting the patience of my readers.

The thirst which is so prominent a symptom at the outset of acute oligæmia may be relieved by suitable drinks (water, carbonated water, lemonade, etc.). The administration of liquids fulfils a twofold purpose: it relieves the subjective craving of the patient, and it helps to restore the blood to its normal volume by supplying one of its missing constituents. Should the patient's appetite be slow to return, or when obstinate anorexia coexists with the chronic forms of anæmia and interferes with the assimilation of nutriment, we may order the aromatic bitters (compound tincture of cinchona, of gentian, etc.), not omitting to take the patient's whims into account so long as he does not ask for things that are positively bad for him.

When the irritability of the nervous system is unduly exaggerated in cases of protracted anæmia—when a hysterical condition is developed, as it occasionally is, nervine medicines may advantageously be combined with our chalybeate remedies. Among the former, bromide of potassium in large doses (from two scruples to a drachm and a half a day for an adult) enjoys a well-merited reputation, in no way lessened by the absence of any satisfactory theory as to its action. Even if we allow that the bromide may be replaced by cheaper salts of potassium (some authors ascribing the therapeutic effect of the bromide to the alkali-metal [Binz, Eulenburg, et al.], we shall still act wisely in preferring that compound which experience has shown to be so efficient, until adequate clinical proof has been given that it possesses no special advantage over its congeners. It sometimes happens that, notwithstanding the gradual disappearance of the symptoms of anæmia, a state of general "hysteriform nervosity," which has grown up during the original disease, persists after its removal. The more clearly this condition of the nervous system assumes the character of an independent sequela, the more appropriate will be the adoption of alterative measures, *e.g.*, the methodical application of cold water in a hydropathic institution, sea-bathing, etc.

As for other sequelæ of anæmia commonly met with in practice, I need only refer the reader to the corresponding chapters of the Cyclopædia (treatment of Pulmonary Phthisis, of Perforating Ulcer of the Stomach, etc.).

Treatment of Intercurrent Complications.

I have already pointed out (p. 409) that anæmic persons are far more liable than those in health to suffer from morbific causes of whatever kind. As they are more likely to contract disease, they ought to take special precautions, so as not to add a fresh malady to that from which they are already suffering. When they are unlucky enough to do so, the superadded affection is usually more severe (p. 411) than in persons previously healthy, and is especially prone to assume an adynamic type at a relatively early stage in its course. This peculiarity is deserving of special attention, and not unfrequently renders it necessary to adopt remedial measures of a special kind to compass a favorable issue. The modifications that have to be introduced into the routine treatment of an intercurrent disease, when it breaks out in a decidedly anæmic subject, are partly negative and partly positive. On the one hand, all weakening measures must be avoided or employed with the utmost reserve. Among such measures are general bloodletting, and when the anæmia is severe, local bloodletting also; drastic purgatives, low diet, iodine and mercury in doses large enough to affect the system, etc. On the other hand, we find ourselves obliged to resort to stimulants and tonics from the outset of the malady. It is not uncommon to see two patients in a ward suffering from one and the same disease, *e. g.*, lobar pneumonia, syphilis, etc., but treated on diametrically opposite principles: the one, plethoric and robust, thriving on heroic remedies; the other, weakly and anæmic, requiring to be handled with the utmost tenderness, lest his fragile constitution crumble away at the first touch.

Chlorosis.

BIBLIOGRAPHY.—*Fr. Hoffmann*, Dissertatio de genuina chlorosis indole, origine et curatione (Edita 1731). Oper. omnium medicorum Supplementum secundum, pars II. p. 389 ff. Genevae, 1753.—*Dahmen*, Dissertatio de chlorosi. 1747.—*Brandis*, Erfahrungen über die Wirkungen der Eisenmittel. 1803.—*Foedisch*, Allgemeine med. Zeitung von Pierer (1832). Nr. 97.—*Blaud*, Revue médicale I. p. 337 ff.—*Roesch*, Med. Annalen. Bd. III. Heft I. (1838).—*Grimm*, Die Bleichsucht, in ihrem ganzen Umfange wissenschaftlich bearbeitet u. s. w. Leipzig, 1840.—*Sam. Fox*, Observations on the disorder of the general health of females, called chlorosis. Lond. 1839.—*Hoefer*, Gazette médicale de Paris (1840). No. 6.—*Gottschalk*, Bemerkungen zur Behandlung der Bleichsucht u. s. w. Köln, 1841.—*Andral*, Essai d'hématologie pathologique. Paris, 1843.—*Buddäus*, Die Bleichsucht, ihr Wesen und ihre Heilung. 1844.—*Becquerel* et *Rodier*, Gazette de Paris (1844). No. 47–51. (1846) No. 26, 27, 33, 36; (1852) No. 24, 25, 26, 27, 30, 31.—*Popp*, Untersuchungen über die Zusammensetzung des Blutes in verschiedenen Krankheiten. Leipzig, 1845.—*J. Engel*, Wiener Zeitschrift, Junih. 1845.—*Forget*, Annal. d. thérap. Nov. 1845; Dec. 1846.—*Henry Marsh*, Dublin. Journ. Nov. 1846.—*Gintrac*, Journal de Bordeaux. Jan. 1846.—*Bauernschmidt*, Die Bleichsucht. Leipzig, 1847.—*Dusourd*, Traité pratique de la menstruation suivi d'un essai sur la chlorose. Par. 1847.—*Ashwall*, Guy's reports A. J. p. 529.—*Valentiner*, Beiträge zur Lehre von der Chlorose. 1849.—*The same*, Die Bleichsucht und ihre Heilung. 1851.—*Boder*, Deutsch. Chr. Vereinszeitschrift. Bd. III. S. 4.—*Henle*, Froriep's n. Notizen. Bd. IX. S. 5.—*Cazin*, Monographie de la chlorose. Gand, 1850.—*H. E. Richter*, Blutarmuth und Bleichsucht. Leipzig, 1850–1854.—*Gendrin*, Gazette des hôpitaux (1851). No. 91, 94.—*Kuechenmeister*, Deutsche Klinik (1852). Nr. 16.—*Cocchi*, Annal. universal. (1853). Aprile e Maggio.—*Rodolfi*, Gazet. Lombard. (1853). No. 7, 8, 9.—*Uzac*, De la chlorose chez l'homme. Paris, 1853.—*Scharlau*, Theoret.-praktische Abhandlung.- Stettin, 1854. Nr. 3.—*Baruffi*, Annal. universal. (1854). Décembre.—*Buechner*, Deutsche Klinik (1855). Nr. 4.—*Putégrat*, Journal de Bruxelles (1855). Février, Mars, Mai, Juin, Juillet, Août, Septembre.—*Rilliet*, Archives générales (1855). Février.—*Becquerel*, Gazette des hôpitaux (1856). No. 3, 4, 12.—*Wunderlich*, Handbuch der Pathologie und Therapie. Bd. IV. (1856), S. 528 ff.—*Ayres*, Americ. med. chir. Review (1857). Sept.—*Roerig*, Archiv für wissenschaftliche Heilkunde (IV). 2. S. 278 ff.—*Morache*,

Essai sur l'anémie globulaire et ses raports avec la dyspepsie. Thèse. Strasbourg (1859).—*Piggot*, Ueber Blutarmuth und ihre symptomatischen Störungen u. s. w. Deutsch von *Haendel*. Weimar, 1859.—*Cazenave*, Journal de Bordeaux (1860). Février. p. 53.—*Burq*, Gazette des hôpitaux (1860). 86 ff., 101 ff.—*Boussard*, ibidem (1861). p. 36 ff.—*Heylen*, Journal de Bruxelles. T. XXII. (1861). p. 87. Janvier.—*Ferrer*, Mémoire sur la chlorose et son traitement. Paris, 1861.—*Flint*, Americ. med. Times (1861). N. S. I. 11.—*Wilks*, Guy's hospital reports. 3. S. V. p. 89.—*Rostan-Siredey*, Gazette des hôpitaux (1861). No. 56, 58.—*Beroud*, De la chloro-anémie et ses rapports avec la surexcitation nerveuse. St. Etienne (1862).—*Cini*, Del sovracccitamento nervoso nelle sue attinenze colla cloro-anemia. Venezia, 1862.—*Biëchi*, Gazette de Strasbourg (1862). No. 1.—*Trousseau*, l'Union (1863). No. 63, 64.—*Orsi*, Dell' anemia della clorosi e della melanemia. Milano, 1863.—*Burq*, Gazette des hôpitaux (1864). No. 30.—*Reiher*, Blutarmuth und Bleichsucht u. s. w. Zeitz, 1866.—*Sée*, Du sang et des anémies. Fascicule I. Paris, 1866.—*Fabre-Suzini*, La chlorose. Marseille et Paris, 1867.—*J. Duncan*, Sitzungsberichte der Acad. der Wissenschaften. Wien, 1867. Bd. LV. S. 416 ff.—*Skoda*, Wiener med. Presse IX. (1862). Nr. 40, 41.—*H. Schulze*, Ueber Chlorose. Inauguraldiss. Berlin, 1868.—*Oppolzer*, Memorabilien XIII. S. 10 (1869).—*L. Corazza*, Storia di un caso di oligaemia con riflessioni su quest' affezione, sulla chlorosi e sulla degenerazione grassosa degli organi.—*Dyes*, Deutsche Klinik (1870). Nr. 2, 4, 6; also (1871), Nr. 6.—*Delioux de Savignac*, Gazette des hôpitaux (1871). p. 88.—*Bouillaud*, Gaz. de Paris (1872). 25, p. 304.—*Hutchinson*, Americ. Journal. N. S. CXXVI. p. 407. April.—*The same*, Philad. med. Times. II. 46. Aug. (1872).—*Morley*, Philad. med. and surg. Reporter, XXVI. 10. p. 222.—*Virchow*, Ueber die Chlorose und die damit zusammenhängenden Anomalien im Gefässaparate u. s. w. Berlin, 1872.—*Ponfick*, Berlin. klin. Wochenschrift. 1873. 1.—*Perl*, Virchow's Archiv. LIX. 1. p. 39.—Further references will be given in the footnotes. See also the chapters on Chlorosis in text-books of Special Pathology.

History.

The term "chlorosis" was used by Hippocrates, and is probably derived from the greenish yellow tint—like that of fading leaves—exhibited by many chlorotic patients (especially by those whose complexion is naturally dark). The intimate connection of the chlorotic state with the development of the sexual apparatus and its functional irregularities in the female sex, seems likewise to have been noticed by the older physicians, as may be inferred from their use of the terms *Morbus virgineus*, *Pallor virginum*, *Fœdus virginum color*, *Febris virginea.* Again, we often find the sallow complexion and bodily languor of young girls ascribed both by ancient[1] and modern writers, medical and non-medical, to love-sickness and unsatisfied desire. This etiological hypothesis is embodied in the terms *Icterus amantium*, *Febris amatoria*, etc. F. Hoffmann was the first to give an accurate description of chlorosis as a separate disease (1731); a description which, notwithstanding his rather one-sided notions concerning its origin, may even now be looked upon as an admirable one. Since Hoffmann's time the malady has been repeatedly described, usually in connection with ordinary anæmia and with more or less reference to the differential diagnosis of the two conditions. The treatises enumerated above are a mere fraction of the literature of the subject. The blood has been examined in chlorosis by Foedisch (1832), Hoefer (1840), Andral and Gavarret (1843), Becquerel and Rodier (1845 to 1852), Duncan (1867); Virchow has recently made a valuable addition to our knowledge of the disease by pointing out the intimate connection of its symptoms with certain abnormalities in the development of the vascular system. The treatment of chlorosis was much advanced by Blaud (1838), who insisted on the importance of a bold and methodical administration of iron; other modes of treatment (*e. g.*, by manganese, as advocated by Hannon and Pétrequin), after enjoying a brief period of delusive popularity, have fallen into deserved oblivion.

Concerning the frequency of chlorosis in former times, we know scarcely anything; during the present century, however, it seems to have grown appreciably more common in Europe (Hirsch). In some countries, especially in Sweden (Huss), chlorosis is certainly known to have spread within the last forty or fifty years. The disease there is almost pandemic, without being at all rare in other countries (England, the Netherlands, France, Belgium, Germany, Italy, Austria, Hungary, Turkey in Europe). In non-European countries, likewise, true chlorosis is very prevalent here and there, independently of other more special forms of anæmia (*e. g.*, malarial cachexia, geophagy or anchylostoma-disease, etc.). Asiatic Turkey stands prominent in this respect (Rigler), together with Algeria (the Moorish population) and the West Indies (the Creole women) [Savaresi]. Hirsch, from whose work these facts are chiefly taken, lays great stress on the difficulties in the way of accurately ascertaining the distribution of the malady, both in time and space, owing to the variable and indefinite denotation of the term "chlorosis." Many cases of ordinary anæmia, as well as the specific forms of the disease alluded to above, are frequently mixed up with true chlorosis in the medical reports we receive from non-European, especially tropical countries; sometimes, indeed, various diseases are actually called by the same name (malarial chlorosis, Egyptian chlorosis, etc.), without being really identical with chlorosis in their etiology, their symptoms, or their morbid anatomy. Hence, it is doubly necessary that we should try to give a short definition of the disease, in order to preclude subsequent misunderstandings, and to obtain a solid basis for our further exposition. I am well aware that any attempt to give a precise definition of chlorosis must, for the present, be highly unsatisfactory, and that my own is not strictly accurate, and at the same time rather arbitrary. Still, it will be applicable to that morbid state which has been clinically known under the name of chlorosis *par excellence*, ever since the term was introduced, though, of course, there was formerly no intimate acquaintance with its histological and other details.

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[1] Cf. *Ocid* (Art. Amator. I. 729); *Palleat omnis amans; hic est color aptus amanti!*

General Account of the Disease.

By chlorosis (chloræmia, chloranæmia) we understand a change in the blood, almost exclusively confined to the female sex, and essentially characterized by a diminution in the amount of hæmoglobin contained in the nutrient fluid. Whether this diminution be chiefly due to a numerical decrease of the red disks (oligocythæmia, in the narrower sense of the term), or to a reduction of the quantity of hæmoglobin in the individual disks (oligochromæmia), as Duncan is inclined to think, must for the present remain an open question. Chlorotic oligocythæmia (or oligochromæmia) is peculiar in its etiology likewise. It frequently coincides with puberty and the early years of sexual maturity in the female. It is often associated with anomalies in the development of the vascular system, among which Virchow assigns the foremost place to abnormal narrowness in the calibre of the aorta and the great arteries generally. Another feature that is characteristic of chlorosis is the readiness with which it yields, either permanently or for a time, to appropriate treatment (by the vigorous use of iron). In this respect it excels all the other forms of anæmia.

These cardinal features are sufficient to give chlorosis an independent place among the general disorders of nutrition (in conformity with the definition on p. 252). But why, the reader may ask, is the description of chlorosis separated from that of the ordinary forms of anæmia? Partly on theoretical, partly on practical grounds, which may, for the most part, be inferred from the few leading facts enumerated above. In the first place, the state of the blood in chlorosis, though very similar to that in anæmia (p. 287), is not absolutely the same; in chlorosis proper the change appears to be strictly limited to the red corpuscles, whereas in anæmia other constituents of the blood, especially the albuminates of the plasma, are likewise modified. Again, the etiology of chlorosis is in many respects peculiar and obscure, and its pathogeny does not admit of being traced, like that of ordinary anæmia, to causal factors with which we are familiar. Finally, the striking effects of suitable treatment on the disease would oblige us, even in default of other reasons, to separate it clinically from other forms of anæmia. The above considerations enable us to understand how it is that chlorosis has so long maintained its individuality in the teeth of all the attempts that have been made to merge it in the great ocean of anæmia. In speaking of its causes, symptoms, and course, I shall have to allude to many additional points that tell in favor of the customary mode of division, and serve to assist us in the differential diagnosis between chlorosis and ordinary anæmia.

The pathogeny of chlorosis being still obscure—the sum of the causes known to us being still inadequate to give us a satisfactory degree of insight into the intimate connection between the morbid processes that constitute the disease—we are driven to adopt an analytical mode of contemplating the subject. It will be necessary, whether in discussing the causes, the morbid appearances, or the symptoms, to avoid everything like *à priori* reasoning concerning the pathogeny of the disease. I shall defer the construction of any more definite view concerning the essential nature of the disease, as gathered from its outward manifestation, until I have exhausted the data furnished by experience. Then, and not before, will a synthetic exposition be possible. That any such attempt must necessarily be imperfect at the present time, the lacunæ in our exact knowledge having to be completed by hypotheses, may as well be stated at once.

Etiology.

Experience teaches that chlorosis is principally due to the operation of certain predisposing causes inherent in the patient's constitution, and therefore of an *internal* kind. Next to these come certain *external* conditions, which also exert a "predisposing" influence by slowly and gradually modifying the constitution of the patient and smoothing the way for the actual disease. When the inherent predisposition and the external conditions just referred to happen to exist together, no special exciting cause is needed to bring matters to a head ; the malady appears to be developed spontaneously, and more or less unexpectedly. In other cases, again, the predisposing causes are reinforced by others, external or internal, of a more accidental kind, whose effects are sufficiently well-known to allow of our assigning them their proper share in the causation of the malady. Cases of this sort, moreover, appear less obscure, for the beginnings of disease are associated with particular events in the patient's life. But, even here, we are compelled to ask ourselves why the accidental noxæ should only give rise to chlorosis in some persons, and altogether fail to affect the health of others. Accordingly, it cannot be affirmed that the causation of chlorosis is the same, or even similar, in all cases ; moreover, we must beware of assigning too high a degree of importance to the majority of those exciting causes with which we happen to be acquainted.

A. *Predisposing Causes.*

Predisposing causes have the largest share in the development of chlorosis. Some of them, indeed, especially those inherent in the constitution, actually stamp the disease with their specific character. Hence, in considering its etiology, we must begin with this class of causes, especially with those to which we have just assigned pre-eminence. As I have already attempted to point out, the tendency to chlorosis varies with age and sex. Indeed, there are many cases in which no other cause can be made out for the disease. Even when other causes assume a greater degree of prominence, the fundamental influence of age and sex is always supreme. For chlorosis is never developed by any combination of causes from which these two essential ones are left out.

1. *Sex.*—Chlorosis is almost entirely limited to the female sex. We occasionally meet with a variety of anæmia in males which, on account of its causes, peculiar symptoms, and course, may unhesitatingly be identified with true chlorosis. But such cases are extremely rare; and I think that many French writers (Usac) have fallen into error by trying to include all cases of anæmia in males, whose origin is obscure, under the head of chlorosis. It would be more correct to limit this term to such cases in the male sex as fulfil the following conditions: (1) absence or inadequacy of the usual causes of symptomatic or of idiopathic anæmia; (2) presence, in a more or less distinct form, of the peculiar conditions that promote the origin of chlorosis in the female; (3) agreement of the aggregate symptoms with those, however peculiar, that are present in chlorotic females. By enforcing the above conditions (essential to the maintenance of chlorosis as an independent form of disease) we shall find the number of recorded cases of chlorosis in the male sex considerably reduced. An old statement of Cantrel's,[1] to the effect that among 160 cases of chlorosis he had collected, *only* 18 occurred in males, would seem to be exaggerated. Cases of supposed chlorosis occurring in oldish men previously in the enjoyment

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[1] Quoted by *Cazin*, loc. cit. p. 20.

of good health (*e. g.*, those recorded by Fouquier[1]), must be viewed with suspicion, for the influence of youth as a predisposing cause of chlorosis is only second to that of sex. Moreover, the cases that are given in full agree more closely with the ordinary type of symptomatic anæmia resulting from dyspepsia than with true chlorosis. Not that I would deny the possibility of chlorosis occurring in men ; I only desire to restrict the term to cases in which the above conditions are fulfilled and in which the disease makes its appearance during, or just after, puberty.

My views on this point are in agreement with those of Tanquerel des Planches ; indeed, I have contented myself with a brief summary of the opinions he expressed a long while ago. After opposing the erroneous statements that had been put forth as to the relative frequency of chlorosis in the male sex (*Presse médicale*, 1837, No. 54) with vigorous and telling arguments, he goes on to describe a well-marked case of true chlorosis in a young man of twenty-one under Rayer's care. The description of the symptoms and the results of treatment are conclusive in favor of his diagnosis. A similar case came under my own notice in the winter of 1873–'74. The following is a condensed record of it :

E. S., a school-boy of seventeen, has always enjoyed good health. He is unusually tall for his age, and has been growing very fast of late. During the last few weeks he has repeatedly complained of feeling very tired, of shortness of breath, and frequent palpitation without cough. His chief trouble is that he gets quite out of breath every time he goes to school from Klein Basel (on the right bank of the Rhine) to the lofty Münsterplatz (on the left bank) ; he has to walk this distance several times a day. Appetite good, occasionally ravenous. Constipation. Spirits very low. No other symptoms complained of. On examination, he is seen to be fairly well nourished, though too tall and slender ; no bagging of the skin such as might result from the removal of subcutaneous fat. Extreme paleness of skin and mucous membranes (lips, conjunctiva). Blowing murmur over the heart ; no signs of hypertrophy ; loud venous hum in the neck. Urine free from albumen ; spleen and lymphatic glands not enlarged ; no fever. Lungs and other organs healthy. Large doses of iron (Blaud-Niemeyer pills) removed all the symptoms within a period of six weeks.

2. *Age.*—Age stands next in importance to sex among the predisposing causes of chlorosis. This malady is chiefly met with in young girls during the period of the sexual evolution, *i. e.*, between the fourteenth and twenty-fourth years of life. Its old name "Morbus virgineus" is not inappropriate, as the

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[1] Journal des connaissances médicales (1834) Janvier—Mars.

adjective is commonly applicable to women at this age. During childhood and before the age of fourteen, chlorosis is rare—at any rate, in the climate of Central Europe; it is equally rare to find chlorosis making its first appearance after the age of twenty-four. On the other hand, relapses are very common when the disease has existed at the time of puberty, and they may continue to occur even in later life. Cases are on record in which the disease has broken out again and again throughout the whole of life (excluding childhood).[1]

Cantrel gives a table of 138 cases to illustrate the comparative frequency of chlorosis in the female sex at different periods of life:

Under 15 years of age	14 cases.
Between 15 and 20	64 "
" 20 " 25	36 "
" 25 " 40	16 "
" 40 " 57	8 "
Total	138 "

He omits to mention whether the cases of chlorosis occurring at an advanced period of life were or were not relapses. It is difficult, moreover, to make out whether cases of ordinary anæmia due to obscure and ill-ascertained causes have been rigorously excluded from this list. Accordingly, we cannot attach any high degree of importance to statistics which are at once of doubtful accuracy and deficient in extent. F. von Niemeyer[2] insists very strongly on the rarity of a first attack of chlorosis after the age of twenty-four. He used to warn his pupils against rashly dismissing anæmia, when it made its first appearance after that age, as "mere chlorosis," and to point out that pulmonary mischief, or renal disease with albuminuria, or a gastric ulcer, might come on with symptoms so deceptively like those of chlorosis as to lead the patient's friends, and sometimes the physician, into serious error. Such warnings from an experienced clinical teacher deserve our most careful attention; we must be on our guard against ascribing obscure forms of symptomatic anæmia in oldish women to chlorosis.

Becquerel[3] and I. Vogel[4] give instances of chlorosis occurring in children. Here, again, it should be borne in mind that we are only entitled to speak of chlorosis in a child when anæmia, in the ordinary sense of the word, has been excluded, *i. e.*, when no sufficient reason can be made out, either in the history or the present condition of the patient, to account for an extreme degree of anæmia in which a deficiency of hæmoglobin is the predominant symptom (p. 500). But this is seldom the case; for a great number of the every-day causes of anæmia are especially prone to bring on the disease—in its ordinary form—in children, owing to the marked susceptibility of the growing organism (p. 302) to impoverishment of the blood. Such cases, of course, ought never to be included under the head of chlorosis.[1]

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[1] *Von Bamberger*, *Virchow*.

[2] Lehrbuch der spec. Path. und Therapie, VIII. Auflage. Berlin. II. 836.

[3] Traité clinique des maladies de l'utérus et de ses annexes. Paris 1859. II., 492.

[4] Handbuch der spec. Path. und Therapie, herausg. von R. Virchow, I. (1854). S. 439.

Though age and sex are unquestionably the most important of the causes predisposing to chlorosis, still there are some other conditions whose influence, subordinate though it be, deserves consideration.

3. *Inheritance.*—An inherited tendency must be admitted to exist in many cases of chlorosis. We often find the disease breaking out in the majority of, or in all, the female members of a family in successive generations and at the same period of life. Now, although there can be no doubt that external conditions of a similar kind, *e. g.*, a similar mode of bringing-up, may often promote the generalization of chlorosis in particular families, and thus stimulate the effect of inheritance, still the existence of the latter cannot be altogether set aside. For, independently of the cases that admit of being explained in the way I have just suggested, there are a sufficient number of others in which no common antecedent condition of an external kind can be discovered for a family proclivity to the disease.

4. *Constitution and habit of body.*—It is generally believed that chlorosis is most common in those girls and young women whose health has been delicate from infancy—whose constitution is of the "anæmic" order (p. 305). Again, an abnormal degree of functional irritability or "irritable weakness" of the nervous system is thought to favor an outbreak of chlorosis when the body approaches maturity. Both opinions are to some extent well founded; it is quite true that chlorosis is very common in persons whose imperfect state of nutrition and habitual paleness indicate a certain degree of persistent anæmia even during infancy and childhood; moreover, the peculiar irritability of the nervous system which I have already described (p. 383) is often associated with those outward tokens of poor blood. Still, it would be altogether a mistake to suppose that chlorosis is un-

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[1] Both *Behrend* (Journal für Kinderkrankheiten, März, 1846) und *Enzmann* (Zeitschrift für Med. Chir. und Geburtshülfe, N. F. III. (1864) 2. p. 73, and 4. p. 196) have fallen into this error.

known among girls who are vigorous and well nourished, and who have never shown any sign of nervous irritability until they reached the critical epoch of long frocks. On the contrary, many of the girls whose constitution is apparently plethoric (p. 308), and whose nervous system has done its work steadily throughout their childhood, become affected by chlorosis. And when the disease breaks out severely and unexpectedly (as it not unfrequently does) in a previously healthy and blooming girl at puberty, the waxy pallor of her skin contrasts very forcibly with the otherwise flourishing state of her nutrition. Moreover, it is in such cases that the nervous irritability of the patient and the singular alteration in her temper contrast most vividly with her behavior when in health. An observer unacquainted with the latter might easily be led to regard the former as her normal mood and as one of the predisposing causes of the chlorotic state. He would thus invert the true relation between the disease and one of its symptoms, and arrive at a totally erroneous conclusion on the subject.

Chlorosis is sometimes said to be more common in blondes than in brunettes (Wunderlich[1]). This must not be taken to mean that chlorosis is at all rare in women of dark complexion; for the malady is very common in dark-skinned nationalities (Italy, Central America).[2] On the other hand, Huss, Berg, and other Swedish physicians assert that the disease is extraordinarily prevalent in Sweden, whose inhabitants are popularly supposed to be fair-skinned and fair-haired, with irides of a light color. Granting the truth of their statements, it would be very rash to connect the prevalence of the disease with the national complexion; indeed, no one has yet attempted to do so (cf. under No. 6, *infra*). I cannot admit, for my own part, that any satisfactory evidence has been adduced for thinking that the prevalence of chlorosis stands in any immediate relation to individual or endemic peculiarities of complexion. Provisionally, therefore, no such relation need be assumed to exist. There is just as little positive ground for connecting a predisposition to chlorosis with other peculiarities of outward habit. The disease is met with in the tall and in the short, in the fat and in the thin; indeed, it shows itself much less particular in the choice of its victims than we might *à priori* have expected it to be.

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[1] Handbuch der Path. u. Therapie. Bd. IV (1856). p. 529.

[2] Hirsch, Handbuch der historisch-geographischen Pathologie. Bd. I. p. 553.

5. *Local errors of development.*—Owing to the all but exclusive limitation of chlorosis to the female sex and the period of approaching sexual maturity, attention has naturally been directed to the behavior of the female generative organs. Some observers conclude that these organs are developed prematurely and enter too soon upon their functions; others, again, that their defective evolution and tardy entrance on their functional activity are causally connected with the occurrence of chlorosis; both, however, agree in thinking that the disease is promoted by some definite and uniform abnormality in the condition of the sexual organs. But the careful observations made by Virchow have conclusively proved that the anatomical state of the generative apparatus of chlorotic women is in no way constant. This is true of the uterus, and more particularly of the ovaries, which were found by Virchow to be sometimes small and ill-developed, sometimes of normal size, sometimes unduly large and vascular. It is quite clear, then, that no definite condition of the generative organs is uniformly associated with chlorosis as a predisposing cause. When I come to speak of the exciting causes of the malady, I shall point out how the state of the sexual functions may contribute to produce it. Their influence will be found to differ in different cases, according to the anatomical condition of the organs.

There is much more reason for the belief that certain abnormalities in the vascular system play an important part in the causation of chlorosis. At any rate, Virchow has long insisted on the causal connection between chlorosis and an abnormal narrowness of the aorta and its branches. He asserts that this defect, which appears to be more common in females than in males, is almost invariably met with in the dissection of chlorotic patients. Moreover, it is an interesting fact that this "hypoplasia" of the vascular apparatus, though occasionally associated with defective development of the rest of the body (dwarfed stature) and, as was pointed out by Rokitansky, with a stunted condition of the sexual organs also, is often found together with a normal completeness of physical development and stature. Even the imperfect condition of the generative organs described by Rokitansky cannot be regarded as constant, for, as Virchow has shown, these organs may vary widely in the degree of their development. Finally, the latter author has called attention to the variable condition of the heart in these cases, this organ being sometimes stunted, sometimes hypertrophied. It will be necessary to enter more fully into these differences in considering the symptoms of chlorosis, for they appear, to a certain extent, to correspond to different clinical types of the disease. The more variable the anatomical characters of the generative organs and the heart appear to be, the more importance does the constant occurrence of arterial hypoplasia assume from an etiological point of view ; for, putting aside the alterations in the blood, this hypoplasia forms the most relatively constant anatomical groundwork of the disease.

The starting-point of this defective development of the great arteries must undoubtedly be traced back to a very early period of intra-uterine life—perhaps to the moment of conception. The tendency to chlorosis would thus appear to be congenital, or to be implanted in a latent form at a very early age (Virchow). But the existence of arterial hypoplasia cannot be regarded, I think, as more than an important predisposing cause of chlorosis ; it does not deserve to be considered as the one essential factor in the production of the disease. It would be difficult, or impossible, to set aside altogether the theory of some primary alteration in the blood, and to derive all the symptoms of chlorosis from the abnormal state of the great vessels. Moreover, the connection between the group of symptoms termed "chlorosis" ever since Fr. Hoffmann's time, and the congenital narrowness of the great arteries, especially of the aorta, is not absolutely invariable, for, although the hypoplasia in question is more common in females than in males, yet it is not very infrequent in the latter (Morgagni,[1] J. F. Meckel,[2] Virchow,[3] and others), without the individuals in question having exhibited the symptoms of chlorosis during life. Again, well-marked chlorosis is extremely common as a temporary ailment of the female sex at puberty; and the average of cases observed during life is unquestionably far in excess of the proportion in which abnormal narrowness of the arterial system is met with on post-mortem examination.

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[1] De sedibus et causis morborum. Ep. XVIII. 2, 4 ; XX. 36 ; XXX. 12 ; LIV. 37 ; LXX. 5.

[2] Hdbuch. der pathol. Anat. (1812). Bd. I. S. 471.

[3] Gesammelte Abhandlungen. S. 688.

Accordingly, the anomaly of arterial development in question cannot be thoroughly fused, either from the point of view of etiology or from that of symptomatology, with our pathological conception of chlorosis. Nevertheless, when it happens to be present in a girl who becomes chlorotic, it must obviously exert a great influence, not only on the causation of the malady, but also, and more particularly, on its severity and its power of resisting treatment. This view agrees very well with Virchow's statement that he has found arterial hypoplasia regularly present in the bodies of chlorotic women on the post-mortem table (*i. e.*, in exceptionally severe cases of the disease); and with that of Bamberger,[1] to the effect that the anomaly of development in question usually gives rise to an "extremely severe form of chlorosis, that is hardly amenable to treatment." Finally, as this error of development, which stands in so close an etiological relation to the blood-change, is essentially incurable, we may accept, for those cases of chlorosis in which it exists, Virchow's[2] view, that the predisposition to the disease is incurable, though it may be rendered latent by appropriate treatment, in conjunction with diet and regimen.

6. *Conditions incidental to modern social life.*—Some of these conditions, to which women are principally exposed, are often accused, with justice, of promoting the development of chlorosis. Foremost among them are neglect of hygienic principles in the bringing-up of women, and the employment of growing girls in unsuitable occupations. Chlorosis is more common in girls bred in towns, among the daughters of the educated classes, than among their peasant sisters. Want of exercise, a

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[1] Lehrbuch der Krankheiten des Herzens. (Wien, 1857). S. 348.

[2] Cellularpathologie. IV. Auflage. (1871). S. 268.

life passed in stuffy rooms, a premature and one-sided cultivation of the intellectual faculties and the emotional nature, at the expense of the body—these are the chief causes that favor the occurrence of the disease. We may take it as proved that chlorosis has increased considerably in frequency since the education of women has assumed its present unnatural direction. In some countries—*e. g.*, Sweden—statistics show that chlorosis has been growing steadily in frequency of late years, its growth keeping pace with changes in the way of bringing up young girls—changes not in the direction of increased simplicity.[1] But we must beware lest we exaggerate the influence of such conditions on the production of chlorosis. It is quite true that the combination of bodily inactivity with intellectual over-exertion, and, still more, with precocious excitement of the imagination by novel-reading and erotic sentimentality, may be to blame, in some measure, for the fact that chlorosis has become quite a fashionable complaint among the female sex; but, although these causes may account for some, they do not account for all cases of the disease. I must protest, more especially, against a view held by many of the public, and even by some members of the profession, who believe the disease always to have its starting-point in erotic ideas. Now, the assertion that chlorosis only shows itself in girls who have no means of obtaining material satisfaction for their desires, is as deficient in fact as it is morally revolting. The old terms, "febris amatoria," "icterus amantium," are certainly adapted to keep up a notion of this sort. All the more forcibly must I call attention to the truth, justly insisted on by Wunderlich, F. von Niemeyer, and others, that chlorosis is not at all uncommon under exactly opposite conditions of education and occupation, and in persons whose ideas move in a very limited sphere. Thus, *e. g.*, the malady is not uncommon in peasant girls, otherwise robust, who show no disposition to morbid sentimentalism, and whose labors in field and garden cannot leave them much leisure for becoming "sicklied o'er with the pale cast of thought." It is also incorrect to regard chlorosis as exclusively a disease of unmarried women

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[1] *Hirsch*, Historisch-geographische Pathologie. I. 556. (1860).

("morbus virgineus"), or to recommend marriage, with its natural consequences, as the best of prophylactic and remedial measures. Usac deserves all credit, both from an ethical and a scientific point of view, for his vigorous condemnation of such crazy theories.

Among the crowd of out-patients who used to attend the Tübingen Hospital in Niemeyer's time, there used always to be a good many robust peasant girls from the surrounding villages, suffering from chlorosis. These girls were certainly not the victims of over-education. Every country doctor in large practice can testify that the rustics furnish no inconsiderable contingent of chlorotic patients. Again, chlorosis is well known to be very common in young women even after they are married. We may accordingly conclude that, although the conditions of modern social life enumerated above do really operate as predisposing causes of chlorosis, their position in this respect is by no means a very prominent one.

7. *Atmospheric and telluric influences.*—Hirsch's account of the comparative prevalence of chlorosis in different countries and continents shows that the malady is independent of diversities of climate. It is endemic both in high and in low latitudes, on the sea-coast and in the interior of great continents. The contrast between the striking immunity of some regions from chlorosis, *e. g.*, north-eastern Russia and Egypt, and its great prevalence in Sweden and Algeria, is sufficient of itself to prove that the distribution of the malady is independent of climate. It appears to be equally independent of season, weather, and the nature of the soil. Some observers, indeed (Wunderlich), have thought the malady more prevalent and severe during the heat of summer; on the other hand, experienced colleagues of mine at Basle are inclined to believe that it is most common during the latter part of the winter and in spring. It remains to be proved how far the increased devotion of young ladies of the better class to "culture" and to social gayeties during the winter months may be to blame for this.

LEEDS & WEST-RIDING CHIRURGICAL SOCIETY

B. *Exciting Causes.*

The foregoing survey of the predisposing causes of chlorosis comprises the greater part of what we know about its etiology. The disease often becomes developed under the favoring influence of age, sex, or one or other of the predisposing causes I have enumerated, without the intervention of any definite exciting cause. Moreover, the exciting causes to which the development of the malady is sometimes attributed, differ widely in the degree of their importance ; some of them appearing to exert a positive influence, while that of others is more or less problematical. I shall now proceed to discuss the exciting causes in question one by one, whether their influence be real or supposed.

1. *Menstrual irregularities.*—While menstruation as a normal periodic function of the female organism cannot reasonably be viewed as an exciting cause of chlorosis, there are certain special epochs in its history, and certain occasional modifications of its course, which may contribute to bring on the disease. Foremost in etiological importance is the period of the first appearance of the catamenia. It may be affirmed, generally, that the earlier menstruation sets in, the more likely is it to bring on symptoms of chlorosis. For instance, girls who, in our temperate zone, begin to menstruate with more or less of regularity in their twelfth or thirteenth year, almost invariably suffer from chlorosis (Niemeyer). Such menstrual precocity is sometimes associated with precocity of bodily development, the girl presenting, at this early age, the characters of mature womanhood, and enjoying excellent health and strength. All the more striking is their subsequent paleness, developed in connection with the other symptoms of a more or less severe, though not usually obstinate, chlorosis. But menstrual precocity is not always associated with a robust constitution and early maturity. On the contrary, it is more often met with as a result of a local formative irritation more or less limited to the generative organs, and bringing them to functional maturity before the rest of the body. Such cases of constitutional debility associated with premature menstruation are more common in towns than in the country. The precocity of the sexual system may, perhaps, be justly attributed to those errors of training to which I have already referred, especially to premature erotic excitement of the imagination. The chlorosis which almost invariably accompanies the onset of menstruation in these cases differs from that last alluded to by its greater severity and obstinacy.

But even when the first appearance of the catamenia is not premature, it may be followed by chlorosis if the body be imperfectly nourished; whereas, in vigorous girls, who begin to menstruate in their fourteenth or fifteenth year, it is decidedly less common. Thus we see that the frequency of the disease, when ovulation sets in at the right time, is largely dependent on the condition of the rest of the body.

Lastly, I must say a few words about the very numerous cases in which chlorosis is associated with delayed appearance of the catamenia. In the vast majority of such cases the chlorosis is not the consequence, but the cause of the delay. The subject is usually a delicate girl, who becomes chlorotic at puberty, either spontaneously or for some definite reason, before she has begun to menstruate; the first appearance of the menses will then be deferred until the disease is partly or wholly cured. Sometimes, though more rarely, the course of events is different; a girl of weak constitution, but otherwise in the enjoyment of fair health, begins to menstruate in her sixteenth or seventeenth year; chlorosis then shows itself, and while this lasts, the menses are suppressed. Finally, there are a few cases of delayed menstruation that deserve especial notice in connection with the etiology of chlorosis. The physical development in these cases is fairly good, but a certain degree of torpor in the sexual domain must be assumed to exist; for the menses do not make their appearance at the expected time, though there does not appear to be any sufficient cause for the delay. The girl may continue to enjoy good health; as a rule, however, she becomes affected by a mild form of chlorosis, coming on without any additional reason. We can hardly do otherwise than ascribe some part in the causation of the malady to the torpor of the sexual organs; and there are circumstances which support this view. For instance, though emmenagogues are generally contraindicated in chlorosis, this class of cases forms an exception to the rule; great benefit being frequently obtained from a judicious combination of tonics with such remedies as are calculated to stimulate the generative functions more directly.

Menstruation may also act as an exciting cause of chlorosi during its subsequent course, though much less frequently tha at its outset. It does not often happen that girls or women who have escaped chlorosis at puberty fall victims to the malady at a later period in consequence of menstruation. But when chlorosis *has* existed at puberty, and when the inherent tendency to the disease is strong (p. 510), relapses are not by any means unusual in after-life, especially at such periods in the activity of the generative functions as are obviously analogous to their first awakening. We constantly see young women who have suffered from chlorosis at puberty, but who have been entirely free from the disease since their marriage—during pregnancy, delivery, and the puerperal state—getting a relapse soon after the re-establishment of the catamenia. This relapsing form of chlorosis must not be confounded with that far more common variety of anæmia which is often brought on by lactation. The former may be distinguished from the latter by the fact that suckling has usually to be given up at an early period, owing to the premature return of the menses and suppression of the milk. Again, the symptoms are so entirely those of chlorosis that the malady cannot be viewed as anything but a relapse.

Peculiarities in the way the menstrual functions are performed occasionally exert an influence on the development of chlorotic symptoms. For instance, when a predisposition to the disease already exists, an intercurrent attack of severe menorrhagia may bring matters to a head. Such cases, however, may always be viewed as complications of chlorosis with acute anæmia, or simply as cases of acute anæmia. The latter may obviously be produced by an excessive menstrual flow, as by any other hemorrhage; and we can only infer that it is complicated by chlorosis when the anæmic symptoms refuse to subside in a regular way, but increase in intensity and persist for an unusual length of time, without any corresponding renewal of the bleeding. Finally, when we see habitually scanty menstruation associated with symptoms of chlorosis, we may regard it rather as their consequence than as their cause; but even here it is quite possible that a moderate degree of sluggishness in the sexual functions may be the primary, while the chlorosis is a secondary phenomenon.

2. *Pregnancy, the puerperal state, and lactation*, are men-

tioned by some writers among the exciting causes of chlorosis. I do not think they deserve the name; or, at any rate, only in exceptional instances. The symptoms are generally due to ordinary anæmia, more or less severe, brought on by the joint operation of these physiological processes and other noxæ, as pointed out in a previous chapter. Lastly, there are a few cases in our medical literature, recorded under the name of "chlorosis in pregnant women," running a severe course towards a fatal issue; these cases ought probably to be excluded altogether from the present category, and assigned to "progressive pernicious anæmia."

3. *Severe intercurrent diseases*, especially chronic gastric catarrh, enteric fever, intermittent fever, acute rheumatism, etc., are sometimes termed exciting causes of chlorosis. What I have said about the influence of pregnancy, the puerperal state, and lactation, will apply, *mutatis mutandis*, to such morbid processes as these. Indeed, the impoverished state of the blood resulting from the latter is even more entitled than that resulting from the former, to be viewed as a form of symptomatic anæmia.

4. *Alterations in the patient's way of life* do really appear to bring on chlorosis in some cases, when a predisposition due to age, sex, etc., already exists. The following are among the chief alterations referred to: *a.* The removal of young girls from the country to a town, with the usual and for the most part unavoidable consequences of such a change of residence (want of fresh air, exercise, etc., late hours and want of sleep, etc.). *b.* Over-exertion with loss of rest at night inflicted on young, growing girls, who have not previously been used to such calls upon their strength. Insufficient food appears to be much less commonly a cause of chlorosis than of idiopathic anæmia.

5. *Moral influences.*—Their importance as exciting causes of chlorosis is generally admitted, and in certain cases cannot be overlooked. But the existence of a predisposition to the disease is an indispensable preliminary in all cases; I allude to that generated by sex and age, as well as by certain abnormalities in the development of the vascular system. Depressing emotions of great intensity though brief duration (terror, anxiety, etc.), and especially the protracted melancholy resulting from disappointed love, home-sickness, etc., seem occasionally to determine the

outbreak of chlorosis. But as the degree of individual susceptibility to such emotions varies widely—being partly dependent on inherited temperament, partly on education—their influence is often so inextricably mixed up with that of the social conditions I have already described (No. 6), that it becomes almost an impossibility to assign their relative value to the predisposing and exciting causes in any particular case. Still, the actual outbreak of the disease occasionally coincides so accurately with certain demonstrable troubles of an emotional kind, that we cannot but ascribe to these a considerable share in its causation.

Pathology.

General Outline of the Disease.

The symptoms of chlorosis may be studied in their least complicated form when the disease shows itself in a previously healthy girl at puberty, soon after the first appearance of the catamenia. In such cases, as I have already said, menstruation usually begins rather early—before or during the fourteenth year. The invasion of the malady is not unfrequently subacute, and, therefore, pretty definite, usually occurring in connection with a particular menstrual period. After the menstrual flow has taken place one or more times, its quantity having been scanty, normal, or abundant, the girl begins to complain, shortly after the termination of a period, of a rapidly increasing sense of lassitude. Anything that requires muscular exertion—going out for a walk, household occupation, etc.—is very unwillingly undertaken; efforts of a more severe kind—running, climbing stairs, lifting or carrying heavy weights, etc.—are speedily followed by exhaustion, and associated with disagreeable palpitation, dyspnœa, and a sense of oppression at the chest. The complexion is simultaneously altered; the natural color of the face and body fades. Girls whose skin is clear assume a waxy transparency of tint; brunettes lose their healthy carnation and present a dirty, yellowish gray hue, with dark bluish rings round their eyes; when these are well marked, the rest of the face looks green by contrast (whence the name "chlorosis," from χλωρός, yellowish green). The cheeks are not always colorless; in some cases of chlorosis as in some of anæmia, a circumscribed flush on both cheeks persists throughout the whole duration of the malady; in the vast majority, however, the face is bloodless, though susceptible of a momentary blush under the influence of emotion or bodily effort. Extreme paleness of the visible mucous surfaces (lips, tongue, gums, soft palate, *carunculæ lacrymales*), and a bluish translucency of the sclerotics, are very characteristic and constant features. Owing to these changes in her complexion, the patient soon presents a peculiar expression of suffering, all the more distinctive as there is no shrinking, no absorption of subcutaneous fat associated with it. A plump face thus comes to look puffy; but it would be a mistake to ascribe its puffiness to œdema of the areolar tissue. A mistake of this sort is almost always due to an optical delusion, to which the physician is specially liable, owing to his habit of inferring the existence of œdema from analogous appearances in the course of other diseases. For the excessive paleness which is so common in chlorotic patients is not usually met with under other circumstances save in association with extreme marasmus or with dropsy; hence the plumpness of the face and body in chlorotic subjects is automatically attributed to œdema by the professional spectator. I may remark, by the way, that dropsical symptoms are extremely rare in chlorotic girls whose health has previously been good; and that, when present, they do not show themselves till a late stage, and are almost always limited to a slight degree of œdema round the ankles. We must, therefore, accustom ourselves to regard any considerable amount of dropsy in a patient believed to be suffering from simple chlorosis as highly suspicious; it is usually a sign of the hypalbuminosis resulting from disease of the kidneys which has been overlooked, or of progressive pernicious anæmia, or, in a word, of some other and more dangerous affection. Finally, it is interesting to note that in many (though by no means in all) cases of chlorosis, the *panniculus adiposus*, so far from wasting, actually increases in thickness, a positive tendency to obesity becoming developed, and disappearing when the chlorotic state is done away with. I shall have to return to this point more than once on account of its theoretical importance.

Such are the appearances presented by simple chlorosis in its early stages. They are far more complicated when the disease attacks girls who are already of anæmic constitution and sickly aspect, or when it precedes and postpones the appearance of the catamenia. Under such circumstances, the period of invasion is longer and more gradual, and the contrast between the patient's normal state and the changes it undergoes in the course of the disease is much less striking. Again, slight dropsical symptoms are relatively more common, though they hardly ever amount to more than slight œdema about the legs and ankles. The disorders of function, viz., the proneness of the muscular system to become fatigued, the dyspnœa and palpitation brought on by exertion, are present and attain their highest degree of intensity in these cases; but the morbid changes are all of them less striking, less likely to rouse attention, owing to the habitual languor and weakliness of the affected person.

Whether chlorosis begin in one or other of the ways described above, it presents the following characters when fully developed: extreme anæmia of the skin and visible mucous membranes, without impairment of the previous state of nutrition (sometimes with an actual increase in the amount of subcutaneous fat); dropsical symptoms comparatively rare, and when present always inconsiderable; power of continued muscular exertion very limited; fatigue speedily experienced; great tendency to dyspnœa and palpitation whenever any considerable exertions are made.

Such are the leading features of the malady. The following deserve brief mention as accessory ones: The respiratory movements are usually rather more frequent (in repose) than they are in health, and at the same time rather more shallow. Chlorotic patients are liable to suffer from a slight, hacking cough without expectoration, which is merely irritative. This cough, associated as it is with pallid cheeks and quickened respiration, may raise suspicions of lung mischief; but the most careful examination of the chest (which ought never to be neglected, and must be performed repeatedly on pain of serious error of diagnosis) fails to reveal the existence of any pulmonary lesion in pure, uncomplicated chlorosis. The pulse is usually small and compressible, often rather quick, even when the patient is at rest; it varies greatly in frequency, and is influenced, just as in simple anæmia, by position, movement, emotion, and other trifling causes. Sometimes, though less commonly, the pulse is harder and more full. The heart's impulse, too, is not always uniform in character, even in repose; usually weak or barely perceptible, it is found in some cases to be permanently exaggerated. Moreover, the heart's impulse varies (like the pulse, but more sensibly) both in frequency and in intensity, the above-mentioned causes giving rise not merely to subjective palpitation, but to an objective quickening, strengthening, and widening of the tangible impulse. At such times we nearly always hear, as we do in anæmic patients, loud systolic murmurs over the heart, especially at its apex—murmurs which may disappear in the intervals of cardiac excitement, or remain audible, though lessened in intensity. The *bruit de diable*, too, described under anæmia, may often be heard in chlorotic patients. Its pathognomonic importance, however, used formerly to be exaggerated. Finally, among the physical signs connected with the circulatory system, I ought to mention a moderate extension of the præcordial dullness occasionally developed in the course of chlorosis, and disappearing entirely on recovery (Th. Stark[1]).

The patient's appetite is sometimes normal, sometimes impaired. She is liable to paroxysms of bulimia and to perverted cravings (picae) for such things as coffee-beans, highly-spiced dishes, salads, and sour articles of food; sometimes for all sorts of indigestible things, such as slate-pencils, lead-pencils, egg-shells, cotton-wool, etc., which she secretly devours. Satiety usually follows close on the gratification of appetite, also a sense of weight at the epigastrium, and eructation of inodorous or sour and fetid gases. Paroxysms of acute cardialgia are by no means rare, and should always make us suspect the existence of an ulcer. But, although gastric ulcer is by no means uncommon in chlorotic subjects (*vide* Complications), still their cardialgia is for the most part of purely nervous origin, and does not result from any organic lesion—the state of nervous system to which the paroxysms are due being closely related to the chlorotic alteration in the blood, the two generally disappearing together. It may be useful to remember that the nervous cardialgia of chlorotic patients, though it *may* occur after food, like that due to gastric ulcer, is more common, upon the whole, when the stomach is empty, *e. g.*, in the morning before breakfast. It is then often relieved — and quickly relieved — by taking food. The bowels are sometimes regular, sometimes — and perhaps more frequently — they are confined. The patient may suffer from obstinate constipation, but diarrhœa is rare, and when it exists may usually be traced to an accidental catarrh of the bowels. The urine of chlorotic patients is pale, of low specific gravity, and contains but little urea or uric acid (Becquerel,[1] Herberger,[2] et al.); its quantity is generally normal. The state of the menstrual function requires especial notice because, as I have already said, the invasion of the malady often coincides with the first appearance of the catamenia and the approach of the female organism to sexual maturity; also because chlorosis is quite as likely to influence menstruation as to be brought on by it. Now, it is a curious fact that the relation of chlorosis to the menstrual function is far from being as uniform as we might expect; indeed, it differs greatly in different cases. These differences have long been known to exist, though it is only of late that their true meaning has been ascertained. In the great majority of those cases of chlorosis in which the malady comes on shortly after the appearance of the catamenia, the menstrual flow grows scanty, or may even cease altogether. In other cases, again, as I have already mentioned in the section on Etiology, the development of chlorosis at puberty retards the establishment of menstruation, and sexual maturity is deferred until the disease is cured or subsides spontaneously. In a third class of cases, again, the menstrual function, already established, undergoes no appreciable check; nay, there may even be actual menorrhagia. Hence, the popular notion—one still held by many physicians—that amenorrhœa is a constant symptom of chlorosis, must be given up. The state of the menstrual function is different in different cases; and, for reasons to which I shall subsequently have to allude, it seems important, and, indeed, indispensable to distinguish on this basis between two forms of chlorosis—an amenorrhoic and a menorrhagic form,—following the lead of Virchow and of Trousseau.[1]

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[1] Archiv der Heilkunde (1863) Bd. IV. S. 46.

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[1] Séméiotique des urines (Paris, 1841). p. 286.

[2] Buchner's Repertor. der Pharmacie, 1843. Bd. XXIX. S. 236, *seqq.*

The important question as to the relative frequency of these two clinical varieties of chlorosis can only be answered by statistics concerning the behavior of the catamenia in a large number of cases. Our present knowledge on this point is derived from the inquiries of H. Schultze. He found that among 64 chlorotic women only 5 menstruated normally, 4 had never menstruated at all; in 7 it was probable that the catamenia, previously regular, had been modified by the development of the malady; the flow had usually been scanty from the first (in three cases copious and abnormally frequent), as well as irregular. Complete amenorrhœa was only noted in 10 cases; hence, it cannot be regarded as a constant symptom of chlorosis. These somewhat indefinite data are based on an insufficient number of observations. They prove, however, that although the catamenia are more often lessened, delayed, or suppressed than unaffected or increased by chlorosis, yet that absolute amenorrhœa is much less common than has hitherto been thought.

Inasmuch as menstruation affords evidence—not, indeed, conclusive, but very probable—of ovulation having occurred, it follows that such chlorotic women as continue to menstruate throughout their illness are capable of conceiving and becoming pregnant. On the other hand, it is *à priori* unlikely that a woman suffering from the amenorrhoic form of chlorosis should become pregnant so long as the amenorrhœa lasts. These anticipations are more or less fully confirmed by experience. We find that in many cases chlorosis is no bar to fruitful intercourse; while, in a still larger proportion, pregnancy is delayed until recovery has taken place. In a very few exceptional instances of amenorrhoic chlorosis, showing an obstinate disposition to recur, the malady may be regarded as, in all likelihood, the essential cause of permanent sterility. Chlorotic patients, like those suffering from simple anæmia, are very liable to leucorrhœa. This symptom may often be ascribed to the chlorosis, as it subsides and disappears with it under the influence of appropriate tonic remedies. Nervous disorders are commonly, nay, very constantly associated with the chlorotic state. They exhibit a protean variety in their manifestations. As in the severer forms of chronic anæmia, irritable weakness of the entire nervous system, with its familiar train of consequences, is the leading phenomenon. It may fairly be argued that not one among the nervous symptoms is peculiar to chlorosis as contrasted with ordinary anæmia; but it is also true that, taken altogether, those symptoms are most fully and definitely developed in chlorotic patients. The exaggerated excitability of the nervous matter and its liability to speedy exhaustion—whether in the domain of voluntary motion, in that of vaso-motor innervation, in that of the special senses, or in that of the neurotic processes of secretion—is never so marked as it is in chlorotic girls; indeed, it occasionally stamps the malady with so decided a hysterical character as to entitle it to the name of "chlorotic hysteria." In the absence of any previous weakness of the nervous system, the purely secondary and symptomatic character of the nervous symptoms associated with chlorosis is adequately proved by their standing and falling together with the latter. They contrast in this respect with the symptoms of ordinary hysteria. The patient's mental state, while the disease lasts, is usually characterized, in an exceptional degree, by fantastic and bizarre caprice. A depressed and tearful tone of mind is habitual to chlorotic persons—not only when the disease begins at puberty, but also, though less markedly, during the relapses occurring at subsequent periods, and in those rare cases when chlorosis occurs in the male sex—rendering their society decidedly unpleasant to their neighbors. It is very doubtful, to say the least, if an "erotic idea" is really interwoven with all the intellectual and emotional phases of a chlorotic girl's existence. The feelings common to humanity must be common enough in young women at the "chlorotic" time of life, even when they are exempt from the disease; and even when love-sickness is really bound up with the melancholy of chlorotic patients, there is quite as much reason for classing it among the consequences as among the causes of the chlorosis. True nymphomania is fortunately very rare, and if the patient's mode of life has hitherto been modest and decorous, the invasion of chlorosis is in no way likely to change it for the worse.

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[1] Journal des connaissances méd. chir. XI. 221.

The metabolic processes going on in the chlorotic organism are usually diminished both in activity and extent, so far as we are able to judge from the lessened excretion of urea. We have no information concerning the production and elimination of carbonic acid in this disease. The temperature of the body is not, as a rule, either raised or lowered (Baerensprung, Andral); and the cases of febrile chlorosis or of severe essential anæmia, with rise of temperature, recorded in medical literature, may be referred partly to errors of diagnosis (failure to recognize incipient phthisis or acute miliary tuberculosis), and partly to "progressive pernicious anæmia" (Biermer). Occasionally, though very rarely, exceptionally severe cases of simple chlorosis terminating in recovery are met with, during whose course febrile paroxysms of considerable, sometimes very great, intensity occur (Wunderlich, Schulze, and others). Such febrile paroxysms are worthy of special notice, as they appear to arise in direct connection with the abnormal state of the blood.

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Anatomical Alterations.

Our knowledge of the structural changes in chlorosis is founded, not so much on the results of post-mortem examination, as on chemical and microscopical observation of the blood during life. Occasionally, an opportunity of inspecting the body of a chlorotic patient, who has succumbed to an intercurrent disease, presents itself. For chlorosis itself rarely terminates in death; though a fatal issue may and does occur when chlorotic subjects are attacked by independent disease of a serious kind, whether this be accidental, or really consequent upon the constitutional disorder.

I shall have occasion to refer, at a subsequent period, to the malignant character that is often displayed by intercurrent maladies in chlorotic subjects, and to the more important complications and sequelæ by which death is sometimes caused. At present, we must be content with a simple recital of the structural changes peculiar to chlorosis itself, avoiding all mention of any other post-mortem appearances, which vary widely in accordance with the nature of the lethal complication.

The body of a chlorotic patient is never much emaciated ; on the contrary, it is usually "well nourished," and the layer of subcutaneous fat is sometimes very thick. All the more striking is the contrast between the plump condition of the body and the paleness of the surface which exaggerates all such differences of tint as may be due to pigmentation. Similar contrasts are evident in the interior of the body, the special color of each organ being rendered peculiarly distinct by the withdrawal of the reddish hue they all owe to the blood. There is no œdema of the soft parts; no effusion into the serous cavities; or, if present, these changes are trifling in degree.

The blood in chlorosis has repeatedly been examined, both in former times and in our own day (Foedisch, Hoefer, Herberger, Andral and Gavarret, Becquerel and Rodier, Duncan, et al.). The results obtained, though differing on minor points, agree on those which are of capital importance. Foremost among the latter is the diminution in amount of the coloring-matter—the oligochromæmia (Duncan, Corazza). This is evident from the brighter color of the blood drawn from a vein during life (Hoefer) ; also from its lessened power of staining (Duncan) ; finally, from the proportion of iron detected in it by chemical analysis (Foedisch, Hoefer, Andral and Gavarret, Becquerel and Rodier, et al.). The percentage of hæmoglobin may sink in well-marked cases of the disease to a half or even a quarter of its normal value, as may be inferred from chemical analysis of the dried residue of red corpuscles (Andral and Gavarret, Becquerel and Rodier). This shows, with some approach to certainty, that the chlorotic condition of the blood is due to some change in its colored elements —the red corpuscles. But whether this change consist in a diminution of their number, or of the proportion of coloring matter contained in the individual corpuscles, is a point still open to discussion in any concrete case of chlorosis (using the term to denote a definite aggregate of symptoms, not an anatomical entity). Either change is *à priori* possible, and both seem actually to occur. Hoefer arrived at the conclusion that chlorotic blood contains fewer red corpuscles than normal blood—that it is *oligocythæmic* in the strict sense of the word; his conclusion was based on the observation that the clot formed by chlorotic blood is usually small, while the percentage of iron contained in it is approximately normal. Further, microscopical examination of single drops of blood showed that the red corpuscles were less closely packed than in a drop of normal blood. Till very recently, the view that chlorosis might always be considered morphologically identical with oligocythæmia was generally accepted, notwithstanding that Popp had long since noticed the paler hue of the individual disks in chlorotic blood. Duncan, however, was the first, by actually counting the corpuscles in two cases of chlorosis, to prove that the other alternative mentioned above was not impossible, viz., that the diminished staining power of chlorotic blood might be due to a reduced amount of hæmoglobin in the individual corpuscles—to an *oligochrosis.* Further inquiries are necessary to enable us to pronounce whether oligocythæmia or oligochromæmia is most frequent as the histological substratum of chlorosis. So far as the symptoms are concerned, a difference of this kind will obviously be immaterial, but it will divide cases of the disease into two categories as regards their pathogeny, and may possibly involve considerations of some importance in relation to treatment.

Foedisch demonstrated long ago that the proportion of iron in chlorotic blood is reduced. In 100 parts of blood taken from :

	Cruor.		*Iron.*
A healthy young man he found…….	13.611–15.000	and	0.880–1.001.
A healthy woman “ …….	12.400–14.000	and	0.801–0.901.
A chlorotic girl “ ……	9.141– 8.590	and	0.330–0.501.

The proportion of iron in the chlorotic blood was barely one-half of that in healthy blood. The lack of iron in the blood of chlorotic patients has since then been confirmed by nearly all observers who have made analyses. Andral found that the number of red corpuscles in chlorosis might be reduced to from 90 to 28 per cent. of the normal number; Usac accordingly distinguishes three degrees of the affection: (1) *Mild chlorosis* (90 to 100 per cent. of red corpuscles, symptoms not striking); (2) *Medium chlorosis* (60 to 90 per cent. of corpuscles, symptoms decided); (3) *Severe chlorosis* (28 to 60 per cent. of corpuscles, symptoms extremely marked). Becquerel and Rodier state that in six cases of chlorosis (1852) the proportion of red corpuscles varied from 109.17 to 45.37; in another case previously examined (1847) it amounted to 49.4; while an examination of the blood of eight healthy women from twenty-two to fifty-eight years of age, undertaken at a still earlier date (1844), gave 113.0 to 137.5 as the proportion of red corpuscles *per mille* in their blood.

Duncan has more recently compared the color of the blood in two chlorotic females and one chlorotic young man (?) with that of healthy blood. The exact proportions he observed were: 0.30 : 0.31 : 0.37 : 1. The depth of color exhibited by the three samples of chlorotic blood was thus only equal to one-third of that exhibited by normal blood. Nevertheless, the proportion of red corpuscles in every one of the four samples placed under the microscope was found to be nearly the same. Their number was about 20,000 in every instance. Hence Duncan concludes that in his three patients the red corpuscles were "oligochrotic"—deficient in hæmoglobin. His view received further support from the fact that the red disks in his samples of chlorotic blood were more slow to sink—were specifically lighter—than those in the healthy blood; this phenomenon being naturally accounted for (supposing the density of the serum to have been the same in all) by a reduction in the heaviest constituent of the corpuscles, *i. e.*, their ferruginous coloring matter.

The remaining constituents of the blood do not appear to suffer either quantitative or qualitative change in chlorosis. This is equally true of the leucocytes and of the albuminates, and constitutes a most important chemical and pathological distinction between chlorosis and anæmia. Whereas in ordinary anæmia, the oligocytosis is associated with hypalbuminosis, the quantity of plasmatic albuminates in chlorotic patients is probably normal; nay, they appear sometimes to develop a condition of actual hyperalbuminosis (Becquerel and Rodier). It is only when the disease is exceedingly severe and has lasted for a long time, and when the attendant disturbance of the digestive functions has begun to interfere with nutrition—in other words, when a symptomatic anæmia is tacked on to the original chlorosis—that we observe signs indicative of a moderate hypalbuminosis. With this exception, the ordinary phenomena of pure, uncomplicated chlorosis are quite inconsistent with hypalbuminosis, and tend to corroborate the evidence obtained from the few analyses of chlorotic blood that have hitherto been made.

The mean proportion of albuminates in the serum of six cases of chlorosis was found by Becquerel and Rodier to amount to 72.1 parts *per mille;* whereas, in the blood of healthy women, it averages only 57 parts *per mille* (Vierordt).

The volume of the blood in chlorosis, if it be diminished at all, is certainly not diminished to the same extent as in ordinary anæmia. Whether there be a positive increase in the total quantity of blood, a *plethora serosa*, as has frequently been asserted, must remain doubtful for the present, owing to the want of direct analytical evidence on the subject. The existence of such a plethora is not by any means impossible, since the volume of the total blood depends on the proportion of water it contains, and this, in its turn, is influenced in some degree by the total quantity of the plasmatic albuminates. Of equal, or even of more importance than the eventuality of a *plethora serosa*, is the possibility of the existence of a so-called *plethora ad vasa* (or *plethora ad spatium*) in a certain class of cases. For, as the capacity of the arterial system is abnormally reduced in many cases of chlorosis, the assimilation of a large amount of albumen may lead to the presence of so great an excess of water in the plasma, as to render the total volume of the blood too great for the vessels in which it is confined (Virchow, loc. cit., p. 10). I shall hereafter point out how a phenomenon of this kind may be made to explain many of the anatomical peculiarities and clinical symptoms of the disease.

Foremost among the alterations of organic structure stand those abnormalities in the vascular apparatus which have been fully described by Virchow. I have already spoken of their causal connection with chlorosis in some detail.

That imperfection (hypoplasia) of the aorta and arterial system generally, which Virchow affirms to be a constant feature in severe recurrent chlorosis, consists primarily in a diminution of calibre. Virchow asserts that in women (more rarely in men) who are otherwise well developed, the aorta may be so narrow as hardly to admit the little finger, whereas under ordinary circumstances, it readily admits the thumb. Rokitansky[1] compares the calibre of the abdominal aorta, in a case of this kind, to that of a normal iliac or carotid artery. Such extreme instances are, of course, rare ; we meet with every possible intermediate gradation in different cases. Next, the abnormal thinness of the arterial walls deserves notice ; indeed, it is necessary to complete the characters of the hypoplasia or arrest of development, by showing that the diminished growth of the vessel in breadth is attended by a corresponding defect in depth. All the layers of the arterial walls, more especially the inner and middle coats, participate in this imperfection, and may be very decidedly thinned. But the vessels are not, therefore (supposing their nutrition to be otherwise unimpaired), more brittle or more easily torn than usual; on the contrary, they are as elastic as india-rubber, returning at once to their previous dimensions after they have been stretched. It may be affirmed that the imperfection in question, when it is not associated (as it often is) with degenerative changes in the inner and middle coats, tends rather to increase than to diminish the natural elasticity of the arterial walls (Virchow).

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[1] Lehrbuch der path. Anatomie. Bd. II. S. 337.

Finally, if the body, as a whole, be stunted, *i. e.*, if the imperfection of the vascular system be associated with impaired development of the entire organism, the arterial hypoplasia will be complete in all its features; the vessels being dwarfed in length, as well as in breadth and thickness. This last anomaly, however, is far less common than the other two, and is only met with exceptionally in chlorotic subjects.

The simple abnormalities of development that I have just enumerated are often associated, according to Virchow, with abnormalities in the origin of the branches given off from the aorta. These are chiefly observed in the descending thoracic aorta, from which the intercostal arteries spring in some irregular fashion; they are relatively more frequent in its upper and middle thirds. Such abnormalities are less common, though occasionally met with, in the abdominal aorta. Upon the whole, a comparison of the recorded irregularities with one another leads us to conclude that they tend more frequently than their normal counterpart to narrow the channel along which the blood must flow—that they are, accordingly, but a more complex manifestation of the simple hypoplasia.

Lastly, among the imperfections that are commonly met with in the vessels of chlorotic patients, Virchow mentions a wavy or trellis-like condition of the intima, whose constituent tissue appears to be alternately thickened and attenuated without exhibiting any coarser alteration in its structure. This irregularity in the thickness of the arterial wall is obviously no more than another manifestation of the abnormal distribution of tissue in space, strictly analogous to the coarser abnormality described just before it, with which it is in fundamental agreement, both as regards its origin and its essential character.

Apart from the anomalies of development presented by the arterial system in chlorosis, we also find anomalies of nutrition. The arterial coats are very often the seat of retrograde changes, among which fatty degeneration of the intima is, according to Virchow, the most common. It shows itself in the form of dull yellow spots or striæ on the surface of the inner coat; they vary in size, and do not project at all, or very slightly, above the inner surface of the artery. Besides these spots, there are also very superficial erosions of the intima, which do not extend to its deeper layers. The spots are most abundant near the origin of the ascending aorta, while, in its descending limb, the striæ predominate, and are almost exclusively limited to its posterior aspect, between the orifices of the intercostal and lumbar arteries. Closer inspection of the spots and striæ, especially at their edges, shows them to be, not homogeneous discolorations, but aggregates of minute dots, every one of which corresponds to an enlarged connective-tissue corpuscle in a state of fatty degeneration.

Far less common in chlorotic subjects than this fatty change in the intima is a fatty degeneration of the middle coat. This structural change, which can only be detected by the microscope, must be viewed (according to Virchow) as analogous to the fatty metamorphosis of the muscular substance of the heart, with which it is usually associated. The latter presents the same peculiar appearances that I described under Anæmia (p. 358); appearances still more strikingly developed in certain forms of blood-poisoning, especially in acute poisoning by phosphorus.

As I have already pointed out in the section on Etiology, the bulk and dimensions of the heart vary not inconsiderably in different cases. In common with the rest of the vascular system, the heart may be stunted in its development; in other cases it may be of normal size, and with normally thick walls; in others, again, we may have dilatation, or even hypertrophy of the left ventricle. A normal or moderately dilated heart appears to be most common; but even true hypertrophy is, according to Virchow, by no means rare in cases of chlorosis with narrow aorta.

There is little to be said about other organs. The principal change they exhibit is the change of color already referred to, which is due to the altered composition of the blood. Traces of fatty degeneration may, however, be detected in the renal, hepatic, etc., cells in chlorosis just as in severe anæmia. In a few very severe cases, in which a so-called "scorbutic taint" has been developed towards the close of life (*vide* the section dealing with the issues and duration of chlorosis), decided tokens of a hemorrhagic diathesis may be found post-mortem: petechiæ and vibices in the skin, hemorrhagic erosions and ecchymoses in the mucous membranes, capillary extravasations in the brain, etc., or even larger effusions of blood into some organ (*e. g.*, the brain) or cavity (*e. g.*, the pericardium).

Considering the intimate relation that subsists between the spleen, lymphatic glands, and marrow of the bones—as cytogenic organs—and the production of red blood-corpuscles, any constant changes found in them would be highly worthy of attention. No such changes are, however, met with; and the few cases of chlorosis in which the spleen has been found enlarged, soft, and abnormally pale (Fuehrer, Archiv für physiolog. Heilkunde, Bd. XV. [1856] S. 67) only illustrate the truth that such changes are in no way constant, but rather exceptional.

As regards the generative organs, I have already stated that they resemble the heart in presenting an extraordinary variety of anatomical development in different cases of the disease. We often find both the internal and external sexual organs (mammæ, pubes, etc.) perfectly normal, even in chlorosis of a severe and obstinately recurrent type, associated with defective development of the arterial system; in other cases, again, the sexual apparatus may be stunted or developed in excess. These differences are most obvious in the ovaries, whose size, vascularity, and richness in follicles may vary within amazingly wide limits (Virchow). The infantile form of uterus is also worthy of notice, when it exists; it may be found long after puberty, and consists essentially in a striking disproportion between the body of the organ, whose development is stunted, and its *portio vaginalis*, which is relatively large. Virchow mentions that in such cases the womb—in sympathy with the imperfectly developed ovaries—may actually be too small for the reception and development of an ovum in its interior.

Further inquiries are needed to determine how far the condition of the heart and that of the sexual organs correspond, *i. e.*, whether defective development of the former is always associated with hypoplasia of the latter, and hypertrophy of the heart with abnormal size and succulence of the parts of generation. Virchow—without committing himself to a positive opinion on the subject—seems inclined to think some such correlation possible; at any rate, he connects those diversities in the functional activity of the sexual apparatus to which I have already alluded as the "amenorrhoic" and "menorrhagic" forms of chlorosis, with differences in the anatomical condition of the heart no less than of the sexual organs themselves.

Special Symptomatology.

(Analysis of the individual symptoms and anatomical alterations.)

It will not be necessary to take up a great deal of space in connecting the individual symptoms of chlorosis with its pathology; for the connection is, to a large extent, the same as that already analyzed under anæmia. On most points, accordingly, a brief reference to what has previously been stated will be sufficient; we shall thus be able to reserve our attention for those other points which are peculiar to chlorosis, and stamp it with an independent character.

The pale or fallow hue of the skin and visible parts, to which the malady owes its name, and which, as may be seen on post-mortem examination, extends to the internal organs likewise, is due to the deficiency of hæmoglobin and the lessened coloring power of the chlorotic blood. That the change of color is far more extreme in chlorosis than in ordinary anæmia may be simply explained by the fact that the proportion of coloring-matter in the blood is usually far smaller in chlorosis than in any save the most intense forms of anæmia. The authors quoted above have found the proportion of coloring-matter reduced to one-half, one-third, or even to one-quarter of the normal average; and such degrees of oligocythæmia (or oligochromæmia) undoubtedly transcend the limits within which the quantitative diminution of the red corpuscles or of their hæmoglobin may vary in simple anæmia. Hence, we may affirm that the chlorotic hue of the surface is the immediate manifestation of the chlorotic state of the blood.

Occasionally, even when the disease is at its height, the patient's cheeks retain a tinge of color; or they may be temporarily flushed by emotion or bodily exertion. This is easily explained if we reflect that the color of the skin depends, not merely on that of the blood, but also on the quantity of this fluid that permeates the cutaneous vessels; the result being also influenced by the more or less superficial position of the vascular stroma. When the skin of the cheeks happens to be supplied with relatively large blood-vessels, it may appear to be permanently injected; when vaso-motor influences cause the arterioles to be relaxed for a moment, or when the heart is temporarily excited, the face of a chlorotic patient may be flushed, notwithstanding the lack of color in her blood. Again, the varying fullness of the cutaneous vessels will be most apparent in persons whose cuticle is thin and delicate, the phenomena of the capillary circulation showing themselves more distinctly through a semi-transparent veil.

The absence of marasmus, the relative integrity of nutrition, and the tendency to *embonpoint* which shows itself unmistakably in many cases, undoubtedly constitute the nucleus of the clinical difference between chlorosis and anæmia, inasmuch as they are peculiar to the former. They likewise furnish indirect proof of chlorosis being independent of such influences as lower the nutrient efficacy of the blood or tend to induce hypalbuminosis; whereas they may easily be reconciled with the presence of oligocythæmia (or lack of hæmoglobin) in its most extreme form. A reduction of the number of oxygen-carriers—of the "respiratory substance" of the blood—must inevitably lead (*cæteris paribus*) to a diminution in the processes of oxidation taking place in the body, and will therefore exert a conservative influence upon the tissues (p. 372). Further, as the attraction of the tissue-elements for the store-albumen of the blood, which they incorporate, decompose, and consume with the assistance of the oxygen—or, in other words, as the activity of corpuscular nutrition—is largely dependent on the stimulant properties of the oxygen contained in the blood—we can readily understand why the primary and excessive oligocythæmia of chlorotic patients should afford a certain amount of protection against hypalbuminosis, even when the supply of nourishment from without is inadequate. Becquerel found the proportion of albuminates in chlorotic blood not only undiminished, but actually increased; and this hyperalbuminosis, when it exists, may be explained by an accumulation in the blood of the albumen derived from the food, and by the relatively sluggish rate at which it is consumed by the tissue-elements. It is not until the digestive organs have begun to suffer in consequence of very severe and prolonged chlorosis that the store of albumen in the blood may gradually become reduced, the supply not equalling the consumption. Then, indeed, symptoms of hypalbuminosis, more especially marasmus, may set in. But the malady is no longer a simple chlorosis; it has become a chlorosis complicated by ordinary anæmia from inanition; slight dropsy may show itself, whereas an entire absence of dropsical symptoms, notwithstanding extreme decoloration of the skin, is one of the characteristic features of uncomplicated chlorosis. But, as I have already pointed out, the conditions previously enumerated are actually realized in a numerical majority of our chlorotic patients; and this explains their small proclivity to dropsy, the absence of any decided marasmus, and the maintenance of their tissues *in statu quo*—facts only compatible with the absence of true hypalbuminosis. Inasmuch, moreover, as the store of albumen in chlorotic subjects is not reduced, but rather (if the supply of food be liberal) increased, and since their blood contains less oxygen than usual, we have two conditions that are eminently favorable to imperfect oxidation of the products which result from the dissociation of the store-albumen, and therefore to an accumulation of fat in the body. The non-azotized compounds resulting from the dissociation of albumen, instead of undergoing conversion into carbonic acid and water, are gradually stored up in the cells of the *panniculus*. This would, in some measure, explain how it is that chlorotic patients not unfrequently grow stouter, their round, pale faces being erroneously called "puffy and œdematous."

The diminished activity of corpuscular nutrition (*vide supra*) will also lessen the amount of the nitrogenous terminal products of tissue metabolism (urea and uric acid). This anticipation is confirmed by the results of urinary analysis in chlorotic patients. The temperature of the body, however, does not, as a rule, sink below its normal level. Its constancy is readily accounted for when we reflect that it depends on two distinct factors—the rate at which heat is generated, and that at which it is given off. The former may be reduced in chlorosis, but the latter depends on a regulating mechanism whose action is not interfered with. I have never myself seen a case of febrile chlorosis terminating in recovery, although the number of chlorotic patients admitted into the Basle Hospital is great enough, and their temperature has been carefully noted during the last few years. I believe that such cases of chlorosis attended with fever are transitional forms between ordinary chlorosis and progressive pernicious anæmia. The presence of fever, or, at any rate, of abnormal elevations of temperature, is quite as great a puzzle in the former as in the latter class of cases. No cause can be discovered for this "anæmic" pyrexia (Biermer) beyond the abnormal state of the blood. I shall have to return to this question when I come to speak of progressive pernicious anæmia; the reader who is desirous of information concerning the probable origin of "chlorotic" fever may therefore consult the appendix to the present chapter.

The fatty degeneration of certain tissues occasionally observed in the bodies of chlorotic patients after death (fatty changes in the heart, the middle coat of the arteries, the hepatic cells, etc.), like that met with in cases of extreme anæmia, may be ascribed to imperfect oxidation of the products of tissue-metamorphosis (cf. p. 373), and thus traced indirectly, like the fatty infiltration of the *panniculus*, to the oligocythæmia. As for the analogous changes that take place in the inner coat of the larger arteries, they admit, in some degree, of a similar explanation. But the narrowing of the arterial trunks, so constant a feature in severe chlorosis, undoubtedly favors their occurrence. The inadequate calibre of the arteries must interfere with the passage of the blood through them; their elastic walls must be stretched forcibly every time the ventricles contract. The mechanical violence to which they are accordingly exposed may act as an inflammatory irritant, and set up active changes in their inner coat—changes that may culminate in fatty metamorphosis and (when the oily *débris* are swept away) in partial erosion of the arterial wall. This mechanical explanation appears to be supported by the fact that the fatty degeneration and the erosion are most marked in those parts of the aorta and its main branches which are most exposed to the impact of the blood.

The cardiac symptoms in chlorosis may be referred partly to the altered composition of the blood, partly to the original hypoplasia of the vascular system. The muscular tissue of the heart requires oxygen, not to meet momentary calls upon its energy, but for any lasting work; but the quantity of oxygen in chlorotic blood is so abnormally small that although the functions and the nutrition of the heart can be carried on under ordinary circumstances—nay, although the heart is capable, upon occasion, of doing a great deal of work for a brief period—yet any call for prolonged exertion involves the risk of speedy fatigue and exhaustion. Now, as the volume of the blood is not diminished in chlorosis, but often actually increased, owing to the hyperalbuminosis, the labor of carrying on the circulation is augmented. This may possibly explain the occurrence of the "chlorotic dilatation of the heart" observed by Stark (*loc. cit.*), which comes on during the course of the disease and does not disappear until the oligocythæmia has been removed. Again, owing to the irritable weakness of the nervous system in chlorotic patients—a weakness in which the excito-motor nerves of the heart obviously participate—paroxysms of cardiac excitement are more readily and frequently brought on than in healthy persons; every such paroxysm being followed by partial exhaustion of the muscular substance of the heart. This explains the great irregularity noticeable in the force, frequency, and other characters of the heart's action. Just after a heaving impulse and a vibrating chest-wall have borne testimony to over-action of the heart brought on by emotional excitement or bodily exertion, we may find progressive enfeeblement and irregularity of impulse, loud systolic murmurs, momentary extension of præcordial dullness, perhaps lividity of the face and jugular pulsation, affording sure proof of acute exhaustion of the overworked muscle. Associated with these phenomena is the subjective symptom which is often so annoying to patients suffering from intense anæmia, viz., a sense of violent palpitation and oppression at the chest; this is analogous to the sense of fatigue in the voluntary muscles when they have been overtasked. I need not once more analyze the mechanism of these and other disorders of the circulation, for they are the same in chlorosis as in anæmia, and depend in either case on imperfect functional restitution of the cardiac muscle, and ultimately on the lack of oxygen in the blood. I have already described the probable origin of the *bruit de diable;* its frequent though by no means constant presence in chlorosis might be taken to prove that in this disease, no less than in anæmia, the total volume of the blood may be reduced and the venous system underfilled in consequence. But, as I have repeatedly said, an exactly opposite state of things (hyperalbuminosis and polyæmia) may likewise exist in chlorosis. How far the presence or absence of a venous murmur in the neck may enable us to judge of the probable volume of the blood (whether increased or diminished) is more than I can say. Neither can I vouch for the correctness of the theory given in the chapter on Anæmia to explain the mechanism of the phenomenon itself. I am free to own that I gave Hamernyk's view as the one generally accepted, without in any degree making myself responsible for its accuracy.

Although most of the circulatory symptoms of chlorosis may be referred, like those in anæmia, to the altered composition of the blood—the two morbid processes overlapping each other and having certain of their features in common; still, many cases of chlorosis possess a character of their own, viz., the arrested development of the arterial system. It is clear that the narrow calibre of the arteries in chlorotic subjects must offer a perpetual hinderance to the circulation, independently of the other phenomena of the disease; a hinderance which may manifest itself most markedly when associated with the oligocythæmia (or oligochromæmia), but which is continually present apart from this. Moreover, it is plain that the degree of the hinderance will vary with the varying volume of the blood. The more blood there is, and the more narrow the arteries, the greater will be the disproportion between the weight to be moved by the heart's contractions and the resistances opposed to its onward movement. Inasmuch, however, as the volume of the blood chiefly depends on the proportion of albumen in that fluid, and this, in its turn, on the supply of nourishment, it is clear, as Virchow points out, that the patient's previous alimentation must exert a decided influence on the amount of labor imposed upon the heart, as well as on the structural condition of its muscular tissue. Every muscle whose functional activity is exalted takes up plastic material in greater abundance, and gradually becomes hypertrophied; to this rule the heart is no exception; accordingly, a hypoplastic condition of the vascular apparatus, when it coexists with a liberal supply of nourishment and a proportionate augmentation in the volume of the blood, must needs be followed by hypertrophy of the left ventricle. Such hypertrophy has actually been observed in chlorotic patients, its existence having been proved, not merely by the usual signs and symptoms during life, but by post-mortem examination (cf. p. 531). On the other hand, should the supply of nourishment be insufficient, and the total volume of the blood correspondingly small, there will be no occasion for the heart to become hypertrophied; it may then be found of normal size or even, like the great arteries, imperfectly developed. Thus we are able to explain, in a fairly simple and yet satisfactory way, the great diversity among individual cases of chlorosis as regards the anatomical condition of the heart and many of the clinical symptoms. Concerning the latter, Virchow expressly states that the thinness of the arterial walls associated with their diminished calibre (so long as they remain exempt from fatty change) tends rather to increase than to impair their normal elasticity; this increase in their elasticity when combined with hypertrophy of the left ventricle, manifesting itself by an increase of tension in the vascular areas at the periphery which may display itself in the form of a "fluxionary diathesis" with a tendency to rupture of blood-vessels and extravasation of blood. This would throw some light on the occasional occurrence of premature or excessive menstruation in chlorotic females; the frequent association of chlorosis with early menstruation on the one hand, and menorrhagia on the other, being thus brought into connection with the state of the heart and arteries. On the other hand, it is equally clear that a precisely opposite condition of the circulation may be anticipated when the volume of the blood is relatively small, the heart backward in its development and the blood-pressure accordingly low; though a chlorotic state of the blood is even more readily developed under such conditions in growing girls than when the supply of nourishment is liberal.

The functional disorders to which the voluntary muscles are liable in chlorosis are similar, upon the whole, to those associated with ordinary anæmia of considerable severity; hence, they do not require any very detailed consideration here. Inasmuch as the chemical processes associated with muscular contraction are not phenomena of oxidation, but phenomena of dissociation of a totally different order (p. 381), it follows that chlorotic patients, although their blood may be very poor in oxygen, will be able to do muscular work—like both healthy and anæmic persons—*at suitable intervals;* they will often be capable of violent, though momentary efforts (*e. g.*, they may stamp their feet when enraged, or dance furiously at a ball for a short time, etc.). But as the functional restoration of the active muscles requires a liberal supply of oxygen, chlorotic persons are just as incapable as those who suffer from anæmia, of continued exertion; hence, their power of doing mechanical work is almost more limited in time than that of healthy people. Hence, too, the feeling of weariness that soon comes on—just as in ordinary anæmia—whose probable origin I have discussed elsewhere (p. 385). This feeling is a most effectual safeguard against disagreeable demands on the muscular system of chlorotic patients, whose behavior is often paradoxical enough to the bystanders. A chlorotic girl

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will be incapable of undergoing any exertion for which she is not inclined, owing to the fatigue it speedily occasions; on the other hand, she will be quite able to undergo the same or even a greater amount of exertion, provided it gives her pleasure. For instance, it is more common for a chlorotic girl to decline some light domestic duty or a short walk, than to refuse to dance at a ball. This contrast of seeming ability with seeming inability ceases to be puzzling if we take into account the different degree of psychical resistance offered by the patient to her overpowering sense of weariness in the two cases. These examples must suffice for the elucidation of the pathology of the phenomena in question.

The other nervous symptoms attending chlorosis, numerous as they are, belong for the most part—like the liability to fatigue after muscular exertion—to the wide domain of "irritable weakness." As regards their pathogeny, accordingly, they resemble the analogous symptoms present in anæmia. But their exceptional intensity in chlorosis is especially calculated to throw light on their origin, by suggesting their intimate relation to the lack of hæmoglobin. Clinical experience, indeed, has shown that "irritable weakness" of the nervous system is especially common in those forms of anæmia in which oligocytosis is a leading factor. We might, therefore, anticipate, *à priori*, that this condition of the nervous apparatus would exist in chlorosis, where the hæmoglobin is often so excessively reduced in quantity.

There are two points, however, that must not be overlooked amid these attempts at explanation. First, that chlorosis is almost exlusively a disease of the female sex; secondly, that it is essentially a disease of the period of sexual development in that sex. Now, we know that the nervous system in women is especially liable to "irritable weakness" and irregularity of tone; so much so, that "nervous symptoms" are more common in women than in men, whatever be the malady from which they happen to be suffering. Further, we know that the female sexual organs often form the starting-point of a morbid erethism ("hysterical," from ὕστερα, the womb) of the entire function of innervation. Abnormal nutritive and plastic processes more often give rise to all the protean manifestations included under the name of "hysteria," when they are localized in the female generative organs, than elsewhere. It is not in any degree fortuitous, therefore, that all sorts of trifling nervous symptoms should very frequently make their appearance in perfectly healthy girls at the revolutionary period of sexual evolution; symptoms more or less decidedly hysterical, and only manifested at such other periods as those of pregnancy, and of morbid disturbance (in function or in nutrition) of the generative apparatus. Should the predisposition to unstable equilibrium of the nervous system due to age and sex be reinforced by a chlorotic condition of the blood, we have every facility for the development of the symptoms of hysteria. Hence it is, that these symptoms are usually more marked in chlorosis than in any ordinary form of anæmia. I believe for my own part that certain bizarre peculiarities, more frequent and more severe in chlorotic than in anæmic patients, and which ought not to be hastily dismissed as phenomena of simple "irritable weakness," are to a great extent nervous seizures whose starting-point is in the generative apparatus, and which are only promoted, not actually caused, by the chlorotic state of the blood. I allude to the moral perversity, the curious likes and dislikes, the craving (*picæ*) for all sorts of queer things, some eatable (coffee-beans), some uneatable (lead-pencils, earth, straw, etc.), which are often displayed by chlorotic girls. For exactly the same symptoms are not uncommonly observed, without any trace either of chlorosis or anæmia, in healthy women during pregnancy, and in patients suffering from leucorrhœa, flexions and versions of the uterus, etc.; to speak more generally, in women whose sexual organs are in any way affected and who become, in consequence, "hysterical."

The respiratory troubles of chlorotic patients are purely functional, and are, upon the whole, very similar to those complained of in anæmia. The accelerated breathing and the slight cough (which so often lead us to suspect lung-mischief) are both of them nervous, and probably depend on abnormal irritability of the respiratory centre and of the sensory nerves of the larynx, trachea, etc. The paroxysmal dyspnœa brought on by exertion is intimately connected, on the other hand, with the disturbance of the pulmonary circulation which ensues immediately upon acute exhaustion of the heart, and gives rise to an accumulation of carbonic acid in the systemic blood (cf. p. 403).

Atony of the digestive organs is as common in chlorosis as it is in anæmia. For its causes, see p. 340. I have already suggested a probable explanation of the perverted appetites and cravings displayed by chlorotic patients in common with pregnant and hysterical women.

The pale and watery state of the urine points, as I have already said, to a diminished metamorphosis of nitrogenous tissue and a diminished destruction of red corpuscles. If we want a theory to account for the pale color of chlorotic urine and its poverty in urea, we must assume that in chlorotic subjects tissue-metamorphosis is not accelerated, but retarded, and that the red corpuscles are not disintegrated at a quicker rate than usual. (Cf. the subsequent section on the "Essential Nature of Chlorosis.")

The interesting diversity in the behavior of the menstrual function, which has recently led to the setting up of two distinct varieties of chlorosis—amenorrhoic and menorrhagic—may be very simply accounted for, according to Virchow, by the differences of structure presented by the genital organs in different cases. He points out that delayed and scanty menstruation, or complete absence of the catamenia, are very probably connected with retarded development or hypoplasia of the uterus and ovaries; premature and excessive menstruation, on the other hand, with early maturity or hyperplasia of those organs. The degree of development attained by the internal organs of generation, and their functional energy, depend in their turn, to some extent, on such accidental conditions as the supply of food, the quantity and quality of the blood, the propelling power of the heart (p. 536), etc., and may therefore be expected to vary considerably in different cases of chlorosis. But they do not exclusively depend on causes *ex*ternal to the genital organs; for the growth and functional maturity of all parts of the body—and, not least, of the female sexual organs—cannot be regarded simply as "mathematical functions" of the variables: alimentation, composition of the blood, and power of the heart. They undoubtedly depend on certain *inherent* conditions of a hereditary order, likewise (viz., the nature of the germinal area in the embryo out of which the generative organs are developed, and the nature and intensity of the evolutionary impulse communicated to it at the moment of conception), *i. e.*, on conditions traceable to both parents. For example, should the earliest rudiments of the genital organs in the unimpregnated ovum chance to be imperfect, or should the evolutionary impulse communicated by conception be inadequate, then neither the utmost liberality of alimentation, nor an abundant supply of blood, nor vigorous action of the heart, will avail to compensate for this aboriginal deficiency. The sexual organs will remain relatively hypoplastic, or will be late in arriving at functional maturity. Conversely, a strong hereditary tendency to sexual completeness may happen to coexist with a deficiency of blood and imperfect development of other parts of the body; under such circumstances we may find menstruation both premature and abundant in cases where we should not otherwise have anticipated any such phenomena. There is yet another cause by which the period of development, the intensity, and the nature of the sexual functions may be influenced—a cause which experience shows us to be common enough, and which consists essentially in peculiarities of innervation. Erotic fancies, and direct stimulation of the sensory nerves distributed to the parts of generation, may give rise to increased vascularity and functional activity of those parts. There can be no doubt that many of the observed differences in the age at which the catamenia make their first appearance, and in their abundance under similar conditions of habit and constitution, ought to be ascribed to influences propagated rather through the nerves than through the blood, though they may secondarily modify the amount of blood supplied to the organs of generation.

Nature and Pathogeny of Chlorosis.

We have hitherto confined ourselves to an analysis of the phenomena presented by chlorosis, without employing the empirically ascertained facts as a basis for further speculations concerning the essential nature and pathogeny of the disease. Still, the reader who looks between the lines will have perceived in what direction I am disposed to seek a bond of union between the causes and the symptoms of chlorosis. I will now attempt to explain my views on the subject more directly, and to deduce the pathogeny of the disease from its essential characters.

The symptoms of fully developed chlorosis may almost all be traced, as I have already shown, to an abnormal condition of the blood, and—to speak more precisely—to a deficiency of hæmoglobin without any corresponding diminution in the albuminates of the plasma. The results of chemical analysis are in harmony with this view; they likewise point to the existence of an oligocythæmia or an oligochromæmia, *i. e.*, to a reduction in the number of red corpuscles, or, at any rate, to a defect in their chemical constitution. The state of the urine—especially its poverty in coloring matter and urea—makes it appear in the highest degree unlikely that the cause of the anomaly in question is to be sought in an increased disintegration of the red corpuscles or a partial removal of their hæmoglobin; it indicates, with an approach to certainty, that the true fault lies in an inadequate renewal of the red corpuscles—sometimes, perhaps, in an arrest of their development, owing to which they do not become thoroughly impregnated with coloring matter.; in either case, to put the matter shortly, in an imperfect evolution of the blood. Of course, I am only speaking of those cases of chlorosis (forming a vast majority) which run an apyretic course, the rare examples of so-called "febrile chlorosis" (p. 535) not yet having found their true place in our pathological system. It is quite possible that in the latter, from the moment that an abnormal rise of temperature sets in, increased disintegration may be associated with hindered development of red corpuscles as a constant result of every variety of pyrexia (p. 339). Even in these cases, however, the fever does not generally set in till the chlorosis is fully established; hence, it cannot possess any constant or essential, but only an accidental significance in relation to the development of the chlorotic change in the blood. I shall have more to say about this subject in the appendix to the present chapter.

Although the usual symptoms of chlorosis invariably indicate that the formation of red corpuscles is hindered or defective, what we know about the causes of the malady forbids us to regard its mode of origin as invariably the same, or, in other words, to affirm that its etiology is uniform throughout. In many cases the disease has its roots at a great depth in the patient's constitution, and therefore shows a tendency to resist all treatment and to recur again and again. In other cases its roots are nearer the surface; it is of a more transient kind, and admits of permanent cure. Although a sort of predisposition may be made out even in cases of the latter class, still this predisposition is of so general a character and so completely within the limits of health, that it cannot be dignified with the name of an actual noxa. Of course, I am alluding to the predisposing influence of age and sex, both of which are of great—nay, of the very greatest importance as causes of chlorosis, and yet are normal attributes of the affected individual, incapable of being classed among "independent morbid states." At most, we are only able to affirm that nearly all chlorotic patients are young (at all events, when the malady breaks out for the first time) and of the female sex; we cannot affirm, conversely, that nearly all young women are or become chlorotic. Sex and age are only "physiological antecedents," not "pathogenic conditions" of chlorosis.

The physiological predisposition due to age and sex may be to some extent, though not perhaps fully, accounted for by reflecting: (1) That the production of red corpuscles is probably less active in the female than in the male, and that the aggregate number of those corpuscles, or, at any rate, the percentage amount of hæmoglobin in the blood, is decidedly smaller in persons of the former sex (p. 296); (2) that at the period of life when chlorosis is most apt to become developed, the female is exposed to conditions which may readily lead to a disproportion between the demand for and the supply of red corpuscles—or functionally active hæmoglobin; for, while the body as a whole is still growing rapidly, the generative organs increasing in size, the vascular system extending both in length and breadth, menstruation frequently sets in, and tends actually to diminish the number of the red corpuscles. We might accordingly anticipat that the critical epoch of commencing menstruation would b favorable to the development of chlorosis, also that the risk would be proportionate to the early appearance and abundanc of the catamenia, to the rapidity with which the body grows, t the rate at which the genital organs approach maturity (p. 513)

But, even before the appearance of the menses, the growth o the body generally, and of the sexual apparatus in particular may make large demands upon the blood ; and the provision o red corpuscles or of hæmoglobin may run short, if for any reason the functional energy of the cytogenic organs is impaired, even without any corresponding deficiency in the alimentation of th organism ; for the production of red corpuscles and of hæmoglobin, though undoubtedly influenced by the supply of nourishment (p. 314), is more or less independent of it and governed by conditions of another order likewise. Among the latter must be included, in the first place, all those external, predisposing and exciting causes which have already been enumerated in the section on Etiology (as we are able to judge, *à posteriori*, from their undoubted influence in promoting the development of chlorosis). Foremost among them are want of exercise, restless nights, premature over-exertion of the mind, and depressing emotions. Of all the causes, however, by which the energy o sanguification and the degree of individual liability to chlorosis is governed, the principal one is the intensity of the original impulse to the proliferation of red corpuscles implanted in th system at the moment of conception, and which continues t regulate the plastic power of the cytogenic apparatus. Whe this is relatively feeble, a predisposition to chlorosis is unavoidable ; this may remain latent for a long time when other circumstances are propitious, but is certain to break out sooner or late as a genuine illness. Should the congenital hypoplasia of th blood be of great intensity, an early attack of severe, recurren and perhaps incurable chlorosis will result from the lack of cytogenic energy. On making a post-mortem examination in the cases we shall often find that the arrest of development was n limited to the formed elements in the interior of the vessels, bu involved the vascular walls as well.

This is the point at which the results of embryology and those of morbid anatomy (whose importance was first distinctly recognized by Virchow) combine to throw light on the pathogeny of many, perhaps of most cases of *severe* chlorosis. The vascular walls and their contents are both derived from the same parablastic tissue of the embryo which furnishes the large group of the connective tissues (His), and which, penetrating from every side into the lacunæ and interstices left between the archiblastic structures, furnishes them at once with a supporting framework and a source of nourishment. The corpuscular elements of the blood are descendants (morphologically and chemically altered) of the parenchymatous elements of the cytogenic organs; they are, moreover, very closely related to those corpuscular elements of the connective tissue from which the inner tunic of the vessels is developed. For the cytogenic organs themselves are nothing more, in the first instance, than lacunar protrusions from the great vascular tree—brood cavities—the outermost layers of whose corpuscular lining are continuous with the inner wall of the vessels, while the inner layers of cells, undergoing progressive multiplication, furnish the rudiments of future red blood-corpuscles. Let us suppose the inborn defect of developmental energy to extend not merely to the blood, but to the corpuscular lining of the vascular tree as well. A hypoplasia of the vascular system will then be inevitably associated with the hypoplasia of the blood, and we shall find those anatomical imperfections in the arterial apparatus which Virchow showed to be constant in cases of severe chlorosis. Lastly, should the failure of developmental energy extend to yet other parts of the parablastic tissue of the embryo, the entire connective substance of the body may participate, to a greater or less extent, in the defective evolution of the blood and vascular apparatus. The development of the skeleton may be retarded and the stature of the body dwarfed. Should the congenital feebleness be restricted to those portions of the parablastic tissue from which the blood and vascular apparatus jointly originate, we shall have those more common forms of severe chlorosis in which the patient's well-grown body betrays no outward sign of the deep-lying fault in her constitution and of the imperfect configuration of important internal organs (the vessels).

I think I have made my views concerning the pathogeny o chlorosis reasonably clear, and have pointed out the line along which further knowledge may be looked for. I am of opinio that, although the problem has not yet been completely solved, i has been brought appreciably nearer to a definitive solution by the results of embryological and anatomical investigation referre to above. Without, therefore, committing myself to a belief tha all cases of chlorosis may be traced to one and the same origin, and fully admitting that the disease may often be a temporary consequence of a temporary disturbance of hæmatopoiesis, nevertheless hold with Virchow that a majority of the severe forms of chlorosis—especially those showing an obstinate disposition to recur—are ultimately due to a predisposition, eithe inborn or acquired at a very early stage of development, and ar therefore incapable of being radically cured.

Complications and Sequelæ.

The ordinary course of chlorosis is not unfrequently interrupted by disorders of various kinds, which cannot be regarde as symptomatic, but assume the position of independent complications. Such disorders are either wholly accidental, *i. e.*, no in any way related to the original malady, or they may be complications in the stricter sense of the word, *i. e.*, the chlorosi may be connected with the secondary affection as its predisposing or exciting cause.

So far as accidental complications are concerned, I need onl say that chlorotic subjects are quite as liable as healthy person to become affected by disease of any kind—mild or severe, febril or non-febrile ; in short, that a chlorotic state of the bloo affords no sort of immunity from the majority of other morbi processes. Concerning the individual character of such accidental diseases, I might repeat what I said on the same subje under anæmia (p. 410). The intercurrent affection frequentl exhibits a mischievous or even malignant character ; febrile disorders, more especially (pneumonia, enteric fever, the acut exanthemata, etc.), jeopardize the patient's life at a relativel early stage in their evolution, by weakening the power of the heart, and so bringing on an adynamic condition of extreme gravity. It is clear, moreover, that the great deficiency of hæmoglobin in the blood—a cardinal feature of chlorosis—introduces a constitutional element of the utmost importance into the history of any serious intercurrent disease.

There are other morbid processes which obviously stand in a much closer genetic relation to the chlorosis. Hence, they are more common in chlorotic than in healthy subjects. They are, as I observed before, true complications of chlorosis. It is interesting to note that some of these processes, setting in during the course of a chlorosis, occasionally outlast it for a variable length of time, thus passing from complications into sequelæ. There are other forms of disease, again, which are sequelæ of chlorosis in a somewhat different sense. They are prone to occur during the after-life of such persons as have suffered from chlorosis in earlier years, especially when the latter malady has recurred. In such cases it is difficult not to attribute the earlier attacks of chlorosis, and the later outbreak of the other disease (whatever it may be), to one and the same original cause, and to view them as joint emanations of the same pathological tendency; thus many of the graver forms of chlorosis may assume a premonitory character in relation to certain ulterior dangers to which the affected individual is exposed.

Among diseases of the respiratory organs, phthisis is closely related to chlorosis. When there is a predisposition to the former, its insidious approaches are often begun under cover of a chlorosis at the time of puberty. As an exciting cause of phthisis, chlorosis would appear to stand on the same footing as anæmia. But it is, unfortunately, too common for the latent pulmonary mischief to be overlooked, physicians and friends alike contenting themselves with the diagnosis of the chlorotic state, and paying no attention to the gradual approach of consumption. Whenever there is the slightest ground for suspecting the existence of a phthisical tendency, either hereditary or acquired, we ought to be most careful; the patient's outward aspect, her temperature, the physical condition of her respiratory organs, cannot be too often reviewed. We shall thus enjoy the consciousness of having done our utmost to avoid error, whatever be the ultimate issue of the case.

Of immediate interest for the just appreciation of the true nature and pathogeny of many cases of chlorosis, is the special liability of the patient (insisted on by Virchow) to inflammatory changes in the endocardium. Such changes are almost always situated in the left ventricle, more particularly (as is the rule in endocarditis) in the mitral valve. Next in order of frequency come the valves of the aorta. Sometimes both orifices on the left side of the heart are affected simultaneously (*endocarditis valvularis mitralis et aortica*). In a few exceptional instances the endocardial lining of the right heart, especially the tricuspid valve, is affected likewise. The liability of chlorotic patients to inflammatory changes in the endocardium is intimately connected with the imperfect development of the vascular apparatus; hence, we find it most marked in those cases where narrowing of the aorta and of its greater branches is present, and the hypoplasia is, accordingly, not restricted to the blood (cf. p. 547). Virchow asserts that, of those cases of early endocarditis which terminate fatally, a relatively large proportion are associated with congenital imperfection of the aorta; further, that pregnancy, and, still more, delivery, are fraught with danger to such patients, who are singularly liable at those periods to suffer from ulcerative endocarditis running an exceedingly malignant course. The comparative frequency with which both mild, and especially severe forms of valvular inflammation in the left heart are found to coexist with chlorotic hypoplasia of the vascular system, leaves us to infer that the valvular endocardium must be unusually vulnerable in such cases. This vulnerability is attributed by Virchow, probably with justice, to the abnormal strain put upon the mitral valve more especially, by the systolic contraction of a hypertrophied ventricle contending with an unduly narrow aorta. The sequence of events is clearly this: owing to the continued mechanical violence to which the valve is exposed, its tissue is thrown into a state of abnormal nutritive irritability; this renders it peculiarly susceptible to the influence of any superadded noxa (rheumatism, septicæmia, etc.); and it is obvious that a very little will often be enough to exaggerate the existing tendency into positive disease. This idea is carried out in fuller detail by Virchow in his original memoirs, which the reader may consult for himself. He will also find it worth his while to refer to those chapters in the present Cyclopædia which are devoted to the pathogeny and etiology of endocarditis.

Among the disorders of the digestive system to which chlorotic subjects are specially liable, perforating ulcer of the stomach deserves a foremost place. I have already observed (p. 411) that this complication is not uncommon in anæmia, and may readily be confounded with simple nervous cardialgia; the error of diagnosis preparing an unpleasant surprise for the physician. It is enough that I should refer the reader to my previous remarks on the subject, reminding him that the relative frequency of gastric ulcer may be brought into connection, in chlorosis no less than in anæmia, with existing imperfections in the vascular apparatus. In the first place those degenerative changes which are even more common in chlorosis than in anæmia, may occur in the arteries of the stomach and lead, first, to spontaneous thrombosis, next to circumscribed necrotic disintegration of the mucous membrane and the formation of an ulcer. Secondly, the degenerative changes in question render the vascular walls unduly fragile; their fragility allows extravasation to take place, followed by circumscribed sloughing of the mucous membrane; this is another way in which an ulcer may be formed. Lastly, it is plain that the risk of extravasation will be heightened by hypertrophy of the left ventricle; the latter, as we have already seen, inducing a "fluxionary diathesis."

The occurrence of cerebral hemorrhage in chlorotic patients may be similarly accounted for; also those other hemorrhagic symptoms which occasionally confer a "scorbutic" character on severe chlorosis, bringing it into a nearer connection (clinically) with progressive pernicious anæmia. Such complications of chlorosis are, fortunately, not very common; still, they do occur with sufficient frequency to show that in the womb of this every-day affection, which is thought so little of, there slumber a legion of dangers, any one of which may, at any moment, bring the patient's life to a premature and unexpected end.

Hysteria is the most common of the nervous complications of chlorosis. I have already pointed out that a certain instability of nervous equilibrium is an all but constant feature of the disease, and may be accounted for, in some measure, by the usual sex and age of chlorotic patients. In many cases, therefore, what we have to do with is not a fresh neurotic complication so much as an integral symptom of the chlorosis. Should the abnormal condition of the nervous system be very marked, especially if it outlast the chlorotic state of the blood, it acquires the dignity of a true complication or sequela. The boundary line by which hysteria, as a symptom, is separated from hysteria, as a complication, is inevitably arbitrary; indeed, we can only feel justified in regarding the protean perversity of the nervous functions as an independent complication, when we have actually observed it to continue for some time after the other symptoms of chlorosis have disappeared—when, in short, it has become a true sequela. But hysteria assumes this independent dignity less often than is usually supposed; indeed, it may be affirmed boldly, that of all the varieties of hysteria, that associated with chlorosis is most amenable to treatment by remedies which remove its cause by modifying the state of the blood.

Choreic paroxysms are not uncommon in chlorotic patients, more especially if they happen to have already suffered from St. Vitus' dance about the period of the second dentition. Epileptic fits are far more rare, though an existing tendency to epilepsy may be greatly aggravated by the development of a chlorotic dyscrasia; indeed, the latter may cause it to break out for the first time. If we limit the term "epilepsy" to those cases in which complete paroxysms, characterized by loss of consciousness and combined tonic and clonic convulsions, occur periodically, we shall certainly have to pause before we affirm that a person who has never previously suffered from them will run any special risk of becoming epileptic, owing to the appearance of chlorosis. But if we include under the head of "epilepsy" (as, after Griesinger's unrivalled account of "epileptoid conditions,"[1] we are perfectly justified in doing) all those slighter manifestations of this terrible disease which consist of "ascending vertigo, sudden terror, momentary loss of consciousness, paroxysmal and involuntary movements of deglutition, etc.," we shall find, in the first place, that they are terribly common, and secondly, that they may not unfrequently pass, after having escaped notice for years, quite suddenly into the typical form of epilepsy. It is in such cases that the development of chlorosis at puberty seems really capable of acting as an exciting cause, and converting "epileptoid conditions" of a mild type, which have been considered beneath notice or entirely overlooked during childhood, into complete epileptic attacks. Sometimes, again, a person who has inherited an epileptic taint, and shown no overt symptoms of it during childhood, will gradually develop epilepsy as she grows up, under the concurrent influence of chlorosis.

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[1] Archiv für Psychiatrie und Nervenkrankheiten. Bd. I. p. 320.

The peculiar neurosis of the cervical sympathetic, known as Basedow's [Graves'] disease is unmistakably connected with chlorosis. Not only is it more common in persons of the female sex (Rosenberg, Taylor, Friedreich, and others), but it is especially prone to occur in young women (A. v. Graefe), and particularly in such as are chlorotic (Friedreich). The connection between the disease and the abnormal state of the blood is further proved *ex juvantibus;* for we often remove the thyroid enlargement, the exophthalmus, and the cardiac palpitation, solely by tonic treatment directed against the chlorosis. Independently of that enlargement of the thyroid body which forms part of Graves' disease, I have occasionally observed a simple, moderate overgrowth of the thyroid in chlorotic subjects which appears to me to depend in some way on the blood-change. I have recently collated a series of observations on young girls in whom the symptoms of chlorosis at puberty were associated with a certain degree of goitre, no sign of vasomotor paralysis in the domain of the cervical sympathetic (exophthalmus, etc.) being discoverable. The thyroid enlargement, indeed, was more like ordinary parenchymatous goitre of moderate intensity; its only peculiarity consisted in its being amenable to the same treatment as that employed against the chlorosis (compounds of iron), without the iodine preparations usually administered in true goitre. Though I am unable to explain the connection between chlorosis and goitre, I have no doubt whatever as to its existence.

All the other neuroses met with in chlorotic patients (*e. g.*, the nervous cardialgia, headache, toothache, backache, etc.), and the local disorders from which they suffer (*e. g.*, leucorrhœa), are equally common in ordinary anæmia, and are, moreover, so indissolubly bound up with the chlorosis itself, that they hardly deserve the name of complications. This is particularly true of the leucorrhœa, which often resists local treatment with successful obstinacy, and yields only when appropriate constitutional remedies are employed to combat the chlorosis.

In reference to this subject, the reader may turn back once more to what I have stated on p. 353 and p. 409. By putting all my observations together, he will find evidence enough to satisfy him that the differences between anæmia and chlorosis—poorness of blood and green-sickness—as regards their complications and sequelæ, are of a decidedly subordinate kind.

Diagnosis.

In setting down any particular case as one of chlorosis, we have first to determine the presence of the more important *positive* signs of the disease; secondly, to exclude such maladies as are clinically allied to it, viz., the various forms of ordinary symptomatic or idiopathic anæmia, and the leukhæmic process.

The chief positive signs of chlorosis are: the patient's age and sex (young girls being, in an overwhelming majority, the victims); the extreme paleness of the skin and mucous membranes, associated with relative integrity of nutrition and absence of emaciation; finally, the predominance of functional over nutritive disturbances throughout the body. The more completely the symptoms can be accounted for by extreme lack of hæmoglobin in the blood (whether as oligocythæmia or as oligochromæmia), without any history of antecedent hemorrhage—the less marked the associated phenomena of hypalbuminosis (marasmus or dropsy)—the more assured the absence of severe organic disease (especially of the lungs, stomach and bowels, kidneys, spleen and lymphatic glands)—the greater the likelihood of the case being one of simple chlorosis, supposing the patient to be of the right age and sex. Even then, however, we must beware of coming too hastily to a conclusion; the patient's history, the state of all her organs and functions, and her temperature, must all be carefully investigated before we can feel confident that our diagnosis is correct. Should there be no history of antecedent bleeding, thus excluding acute anæmia from among the possible causes of the existing bloodlessness; should the evening temperature be normal; should there be no sign of early phthisis in the apices of the lungs, none of gastric ulcer or of gastro-intestinal catarrh; should the disturbance of digestion be simply due to atony of the digestive organs—then we may decide in favor of chlorosis, and treat the case accordingly. Our decision will be confirmed by finding the urine invariably free from albumen, the spleen of normal size, the lymphatic glands not swollen, and no excess of leucocytes in the blood. In this way, *per viam exclusionis*, keeping all the possible causes both of ordinary anæmia and of leukhæmia in view, we may satisfy ourselves of the existence of true chlorosis even if the patient happen to be under or over the usual age. When we suspect its presence in a patient somewhat advanced in life, it will be necessary to ascertain whether she suffered from undoubted chlorosis at puberty and at various subsequent periods, or whether the existing attack is the first of its kind. Should the latter be the case, the extreme rarity of a first attack of chlorosis after the age of twenty would lead us to suspect the correctness of our original diagnosis, and to search with redoubled vigilance for other causes of anæmia (especially disease of the stomach and kidneys). On the other hand, if we get a history of repeated outbreaks of chlorosis since puberty, it will be *à priori* probable that we have to do with a relapse occurring in a constitution aboriginally predisposed to the disease. In such cases the vascular apparatus is usually imperfect, so that we may even infer the existence of such imperfection during life. A deeply-rooted and probably inborn predisposition to chlorosis, associated with hypoplasia of the vascular system, may also be inferred when we discover symptoms of chlorosis coming on *before* puberty—

during childhood; symptoms incompatible with ordinary anæmia, and indicating a deficiency of hæmoglobin only. A similar conclusion will also be legitimate when we find an aggregate of peculiar symptoms, which we are obliged to term chlorosis, occurring spontaneously in a person of the male sex. I need hardly say that our scruples will be diminished if the man be young—about the age of puberty; for the sexual evolution taking place at this period is favorable not only to the blood-change in question, but also to the development of nervous instability of a hysterical (*sit venia verbo*) type. We shall be all the more inclined to view a peculiar form of "anæmia" in the male as the analogue of chlorosis in the female, when we find not merely the blood-change, but the abnormal condition of the nervous system, and the bodily state generally, in some degree analogous to those displayed by a chlorotic girl.

It is of importance, as regards the patient's prospects of future health, that we should know, with more or less of certainty, if imperfect development of the vascular apparatus is associated with the chlorosis. Hence, we want some other more direct signs of this condition than those derived from the premature occurrence of the chlorosis itself, from its obstinacy and recurrent character, etc. The following may perhaps deserve to be regarded in this light: (1.) Imperfect development of the body as a whole, due to hypoplasia of the skeleton, such as is not unfrequently met with. (2.) Delayed arrival of the generative organs at functional maturity. This is still more common. Under this head may also be mentioned the arrest of those peculiar local changes in the mammæ, pubes, axillæ, etc., that are so intimately connected with the sexual maturity of the feminine organization. (3.) Premature and excessive menstruation, when associated with signs of hypertrophy of the left side of the heart, without the presence of any valvular mischief, kidney-disease, or other cause to account for the hypertrophy. (4.) Accompanying the foregoing symptoms there may be a systolic murmur, audible about the origin of the aorta and along the ascending portion of the arch. Such murmurs, of course, will only be generated if the vessel is unequally contracted, and the blood has to force a passage through a disproportionately narrow channel somewhere in the first part of the aorta. Inasmuch, however, as the calibre of the vessel is usually narrowed in a more uniform manner, we need not expect to hear a murmur very often.

How chlorosis may be distinguished from progressive pernicious anæmia will be discussed in the appendix to the present chapter.

Duration, *Issues*, *Prognosis.*

The duration of chlorosis is singularly variable. This is partly due to the effects of treatment, partly to the varying character of the disease itself in particular cases.

There are very few affections whose duration is so greatly influenced by remedies as that of chlorosis. Its graver forms, when left to themselves or treated hesitatingly or improperly, show not the slightest disposition to get well spontaneously, but may persist with undiminished intensity for years together. Its milder varieties, for which we do not find it necessary to assume any deep-rooted constitutional cause, and which admit of being readily and permanently cured by suitable remedies, usually run a very slow course when let alone. When homœopathy was at the height of its popularity, many such "chronic cures" of chlorosis came under observation. The health and strength of the unlucky patient were profoundly damaged for many weeks or months. Even at the present day, when we come across any of the mystical adherents of that singular doctrine, we may fairly offer every new case of chlorosis as a test of the efficiency of their therapeutic method. It may be affirmed, generally, that every form of chlorosis—even that which begins in a subacute fashion and runs a mild course (p. 517)—tends to become chronic, and that, without appropriate treatment, it is almost certain to prove tedious.

Of course I do not mean to question—on the contrary, I wish to lay stress upon—the fact that the malady lasts longer when it is severe than when it is mild, whatever the treatment adopted. Even the removal of the functional disturbances caused by the abnormal state of the blood, and the improvement of the patient's complexion by the use of chalybeate medicines, is a far more tedious business when the malady is severe, when the tendency to it is ingrained and inborn. Still, even in such cases as this, vigorous and persevering treatment will be crowned with a measure of success denied to the physician who loses heart; that is, it will succeed in curing the patient for a time, understanding by the term "cure" a removal of the abnormal paleness, and a restoration of normal capacity for exertion. But a radical and permanent cure can only be looked forward to when the hypoplasia of the blood is of a more intercurrent kind—when it is chiefly due to outward causes. We must expect the disease to recur once or more than once, whenever we are able to infer (from the symptoms described above) the existence of congenital imperfection in certain tissues (the vessels and the formed elements contained in them).

What I have just stated shows that chlorosis often issues in complete and permanent recovery; often, too, in recovery, complete or partial, with the probability of a relapse; also that neither of these favorable issues can be expected without employing energetic and suitable therapeutic measures. Should the latter be omitted, chronic ill-health will usually be the patient's lot, and may drag on to a relatively advanced period of life. In the graver forms of chlorosis the patient's health can only be maintained by art, *i. e.*, by the almost uninterrupted administration of specific (ferruginous) remedies. I know women who have been obliged to take iron for years, in order to continue free from chlorotic attacks. This uninterrupted use of iron does not in any way impair their general health; on the contrary, they feel well and lively so long as they are taking it; their complexion is fresh and blooming, and they are quite equal to all the claims of domestic and social duty. Whenever they try to leave off their medicine, they immediately begin to suffer from symptoms of chlorosis, and find themselves compelled to resort once more to their "tiresome pills." No one will question that this artificial health, such as it is, is better than no health at all, or that the issues of chlorosis are more favorable, upon the whole, than those of many other constitutional maladies.

Death, in chlorotic patients, is nearly always a result of complications or sequelæ (*quas vide*), seldom of the chlorosis itself. The true place in our pathology of those cases of "malignant chlorosis" which are scattered through our literature—cases in which febrile symptoms and hemorrhages occurred, and which ended fatally—has been rather doubtful since we have learned to recognize progressive pernicious anæmia; for they probably belong—or, at any rate, some of them—to the latter category.

Among the accidental complications of chlorosis, intercurrent febrile disorders (pneumonia, typhus, etc.) commonly lead to death with symptoms of exhaustion. Of those complications, on the other hand, which are genetically connected with the chlorotic process, perforating ulcer of the stomach with diffuse peritonitis, and cerebral hemorrhage, are the most likely to prove fatal. The most malignant among the sequelæ of chlorosis are phthisis (not at all uncommon), and endocarditis—especially when it comes on after delivery. Upon the whole, therefore, a favorable issue can only be guaranteed in chlorosis when the disease is uncomplicated, and can only be considered probable so long as there is no immediate risk of complications setting in.

Such, then, are the grounds upon which our prognosis must be based. It would be premature and incorrect to give an absolutely favorable prognosis in all cases indiscriminately, simply because the results of treatment are usually so brilliant. We are only entitled to give a hopeful opinion *quoad valetudinem futuram*, when we are able, for the reasons mentioned above, to exclude any rooted predisposition to the disease (when the chlorosis is of a *mild* kind). When the symptoms, on the other hand, point to the existence of vascular abnormality—especially if the disease has already recurred more than once (*severe* chlorosis)—then we must confine our favorable prognosis to the patient's prospect of life (*quoad vitam*). The prognosis is positively unfavorable, or, at all events, doubtful, when complications exist; especially if the patient is unexpectedly attacked by some acute febrile disease. Indeed, the mere possibility of grave complications or sequelæ (phthisis, endocarditis, gastric ulcer, etc.) ought always to be present to the mind of the physician, even when he is dealing with a case hitherto uncom-

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plicated. But if we set aside those possibilities, we may venture, in view of the probable effects of vigorous treatment, to give a hopeful prognosis in uncomplicated cases, so long as there are neither febrile exacerbations nor signs of a hemorrhagic diathesis to approximate the chlorosis to progressive pernicious anæmia.

Treatment.

From what I have already said about the causes of chlorosis, it is plain that any prophylaxis, or any fulfilment of the *indicatio causalis*, can only be attempted within very narrow limits. Since the malady is often—especially when severe—the expression of a congenital hypoplasia of a particular class of tissues, aggravated by age and sex into positive disease, it is obvious that such ingrained pathologico-physiological conditions can neither be prevented nor eradicated. Hence the prophylaxis and the causal treatment of chlorosis must be limited to the modification and removal of those factors which are often accessory to the development of the disease, or favorable to its evolution, and which mainly consist, as we have already seen, in a wrong way of living—in unsuitable occupation both of mind and body. I have already alluded, under the prophylaxis of anæmia, to the points which are of most importance in this connection ; it will only be necessary for me, therefore, to make a few explanatory additions to my previous statements.

So far as there is any prophylaxis of chlorosis, it must consist —especially if we have reason to fear the existence of hereditary or inborn predisposition—in endeavoring to strengthen the constitution of a girl during her childhood, and particularly at the critical age of puberty, by appropriate training. Those measures should be preferred which we know from experience to be calculated to increase the energy of molecular change and the activity of the organic functions—especially that of sanguification. Young girls who are likely to suffer from chlorosis, or who have already suffered from it, must be liberally supplied with food rich in cytogenic material ; when possible, therefore, with meat. Farinaceous and saccharine food, dishes containing much gelatin and fatty matter, and culinary dainties, are less suitable; nay, they are even to some extent contra-indicated, inasmuch as they tend to retard tissue-metamorphosis. Hence, the common practice of ordering a milk-cure in spring and a grape-cure in autumn is less useful in chlorosis than a strict injunction that the child, girl, or woman should eat a slice of juicy meat, either roasted or boiled, every day, whether she wishes it or not. Further, young women whose constitution is of the relaxed type, and whose blood is renewed too slowly, should be compelled to take open-air exercise daily, even in the winter months; when they are confined to the house, they must devote themselves more to domestic work than to any sedentary occupation such as sewing, reading, music, etc. When opportunities for exercise are lacking (as in great cities and among the so-called "upper" classes), they may take lessons in gymnastics or in swimming. But these hygienic efforts must not be excessive; we must bear in mind that the formation of red corpuscles is promoted by moderate exercise, not by over-fatigue of the muscular system, and that bodily movement is only beneficial when it becomes a daily habit at regular intervals. Moreover, it is of the last importance that sleep should not be interfered with. Nothing does more to check the healthy development of a youthful constitution than sitting up at night; the sleep thus lost is but imperfectly made up by broken rest during the ensuing day. Important as bodily activity unquestionably is for young ladies with a predisposition to chlorosis, that activity must not consist in going out every night to balls and parties, and returning home long after midnight to seek inadequate repose by way of preparation for renewed exertion of a similar order on the morrow. Social excesses of this kind are most prejudicial to the health of girls and young women, and promote, as experience shows, the development of chlorotic symptoms; on the other hand, it would be both cruel and needless to forbid all balls and parties to young people merely because they happen to be predisposed to chlorosis. So long as rigorous measures of this sort are not enjoined by special features of the case (*e. g.*, a tendency to lung-mischief, cardiac symptoms, etc.), we need not place an occasional appearance in society or at a ball upon our index; such innocent pleasures may be allowed in moderation.

Again, as I pointed out in speaking of anæmia, very hot weather undoubtedly exerts a relaxing influence upon the constitution, interferes with sanguification, and may, therefore, increase a predisposition to chlorosis. When such predisposition exists, and circumstances permit, prophylactic measures should be adopted. What these measures are, I have already stated (p. 429). I may add here that, besides spending the summer months in Alpine neighborhoods, chlorotic ladies whose home is in a city or in a low-lying inland region may derive great benefit from removal to our northern seaboard. In mountain villages, they are braced by the climate, and their nutritive processes are stimulated by walking exercise, climbing, etc. At the sea-side, bathing and exposure to the impact of the waves exerts a still more powerful influence on nutrition, an influence hostile to the development of chlorosis in a relaxed organization. But, whether the patient be sent to the hills or to the sea, it is of real importance that she should be withdrawn for some weeks from her usual surroundings, and allowed to live a more natural and freer life. For there can be no doubt that the claims of so-called "culture" press very heavily at the present day on young girls. They are more often sacrificed than they used to be, to a systematic training of the intellect and the emotions, whose primary and unsatisfactory results are self-asserting omniscience and gushing sentimentality. I have already said that a training of this sort is very prone to make an existing predisposition to chlorosis culminate in an outbreak of the disease; hence, a temporary removal from home and home influences is likely, apart from anything else, to produce a good effect on the health of a young girl. For, without saying a word in favor of those singular "resorts for the air-cure," the dreary monotony of whose scenery is only matched by the rude accommodation, food, and society, provided for visitors, I can affirm confidently that a summer spent in some pleasant locality among the hills, at the sea-side, or elsewhere — quite apart from any of the collateral advantages that may be derived from air, exercise, bathing, etc.—often affords a young lady her only chance of escaping for a time from the shackles of her conventional home-life and the burden of superfluous ideas, emotions, æsthetic and scientific aspirations, etc., she is made to carry. Care must be taken that the good effects of the change are not too speedily effaced by a return to the usual routine of winter life, with its close rooms, lessons, concerts, and social amusements, and that the girl's life at home should be regulated in accordance with nature and common-sense.

In former years, when a causal connection was believed to exist between chlorosis and the birth of sexual appetite and erotic fancy (cf. the terms *morbus virgineus*, *pallor amantium*, etc.), it used often to be a question whether early marriage with its natural consequences might not prevent the disease. In my opinion, only a cynic would ask such a question at the present day; for, even allowing that the causal connection were really proved to exist in a majority of cases, there would remain strong objections on the score of morality against recommending marriage on such grounds as this. As a fact, however, there is no shadow of justification for the belief that the erotic instincts of such girls as become chlorotic are at all stronger than those of their healthy companions (cf. p. 523). Moreover, experience shows us that a deep-seated tendency to chlorosis cannot be eradicated by the usual consequences of matrimony; for the disease recurs again and again in a vast number of married women, both young and middle-aged (p. 511). Lastly, many women who suffer from temporary chlorosis in girlhood, grow into old maids without any return of the disease. It is plain, therefore, that marriage is no more a preventive of chlorosis than failure to gratify sexual appetite is a common cause of the disease. Medically, therefore, we have no reason to recommend early marriage for such a purpose; and we may hope that both the public and the profession will gradually arrive at more decent opinions concerning the origin of chlorosis.

Still, we now and then meet with cases in which marriage is advisable—not indeed as a preventive measure—but with a view to the fulfilment of the *indicatio causalis*. In speaking of the exciting causes of chlorosis, I pointed out (p. 516) that emotional influences, especially of a depressing kind, might be among them. Thus, *e. g.*, when a predisposition already exists, unrequited affection, or a love-affair nipped in the bud by parental interference—in a word, disappointed love—may produce chlorosis in a young girl. So too home-sickness, disagreeable surroundings, and other depressing influences may act in a similar way. Should the physician succeed in discovering and removing the cause of depression—*e. g.*, in the first-named instance, by overcoming the parents' dislike to their daughter's marriage—he will thereby fulfil the *indicatio causalis* in the particular case, and possibly help to cure the chlorosis. In other cases of an analogous kind, the relief of nostalgia by sending the patient home, or effecting some favorable change in her circumstances, may with equal right be included among "remedial measures."

But I need not linger over the fulfilment of the *indicatio causalis;* it consists, after all, only in the removal of accessory causes, while the true cause of the disease cannot—in really severe cases—be in any way eradicated. So far as these accessory causes of an outward kind exert a *predisposing* influence and are connected with a wrong mode of life, the measures to be adopted against them are the same as those I have described under the head of Prophylaxis. Of the *exciting* causes (among which the depressing emotions just alluded to may be classed) the most frequent one, viz., commencing menstruation (p. 513), cannot be prevented in the interests of an existing chlorosis. We are not acquainted with any means of arresting that periodic function, once established, which would not be followed by grave consequences. Further, it is a question how far we ought to interfere with the amenorrhœa that so commonly sets in during chlorosis by administering emmenagogues; also, if we ought to meddle with the menstrual function when its appearance is unduly delayed (till the sixteenth or eighteenth year, or even later) by the chlorosis. For the vast majority of cases these questions may be unhesitatingly answered in the negative, for the amenorrhœa and the delayed appearance of the catamenia are both of them, as a rule, *consequences* of the chlorosis, which may best be made to yield by appropriate specific treatment of the primary disease; they cannot be viewed as its *causes*, requiring to be removed as a preliminary measure. In a very few cases, when an obstinately recurrent chlorosis is associated with extreme delay in the appearance of the catamenia (later than the seventeenth year), we may possibly find it desirable to give mild emmenagogues in conjunction with a systematic course of roborant treatment, for the activity of the cytogenic organs must obviously be affected by the state of the generative function no less than by various other causes. Observations on castrated males and spayed females (both of the human species and among the lower animals) show that a certain degree of oligocythæmia —a relaxed type of constitution, with a tendency to put on fat —results from artificial suppression of the sexual functions. Now, if the chlorosis be associated with unusual torpor of the reproductive system, manifesting itself by the absence of any sign of menstruation in girls of seventeen or eighteen, there can be no reason against our assuming provisionally that gentle stimulation of the generative apparatus by the milder emmenagogues may exert a favorable influence on the hypoplasia of the blood and the chlorotic state as a whole. In such cases—and in such cases only—I can recommend the addition of aloetics to ferruginous compounds from personal experience of their usefulness.

I usually prescribe reduced iron with aloes in a pilular form for such cases. In the vast majority of cases of chlorosis, however, I rather avoid giving aloes on account of its emmenagogue properties, *e, g.*, when I want to relieve the habitual constipation of chlorotic patients by means of compound laxatives.

Great as may be the value of the prophylactic measures described above, much as we may desire to fulfil the *indicatio causalis* when the disease is already present, there can be no doubt that our chief duty in any case of chlorosis, whether recent or of long standing, whether mild or severe, whether a first attack or a relapse, consists in a prompt and energetic fulfilment of the *indicatio morbi.* For all the measures hitherto described for the prevention or the radical cure of the disease often turn out inadequate; the chlorosis comes on in spite of them, and once developed it usually persists under a plan of treatment exclusively dietetic. On the other hand, remedies calculated to alter the composition of the blood almost always enable us to achieve a brilliant, though often only temporary success, even in severe cases and under the most unpromising conditions. The bold and free use of iron is of more importance than a meat diet, exercise, sleep, a country life, sea-bathing, mountain air, regulation of the emotional life. I do not hesitate to say that a couple of boxes of steel pills or any other active preparation of iron will do a chlorotic girl more good than the most complicated plan of treatment in which iron occupies only a subordinate place or is postponed to a long course of "preparatory treatment."

There is scarcely any point in therapeutics so fully established as the remarkable efficacy of iron in removing all the symptoms of chlorosis. In other forms of disease, attended by anæmia, this metal may be a valuable resource, but in none is its beneficial effect so immediate and dramatic as in true chlorosis. Moreover, as I have already pointed out, a course of "preparatory treatment" is really necessary in many of the symptomatic forms of anæmia before we can proceed to order iron; the remedy may for a time be contra-indicated by the presence of severe dyspepsia or of fever, which have to be got rid of in the first instance. Moreover, when the oligocythæmia is associated with any marked degree of primary and secondary hypalbuminosis, a great variety of "roborant measures" must be employed (*e. g.*, suitable diet) in conjunction with iron if the anæmic symptoms are to be subdued. On the other hand, the more sure we are that a given case is one of true chlorosis, the more confident we are that it is not one of symptomatic anæmia due to some latent vice of constitution, or of chlorosis combined with ordinary anæmia, the more certain will be the effect produced by the immediate and exclusive administration of iron. Niemeyer, in his masterly chapter on the treatment of chlorosis,[1] says very justly that when the disease is uncomplicated, elaborate directions about diet, exercise, etc., are superfluous; we need not force the patient to take quantities of meat or milk against her will, or make her weary herself with tedious walks; we need only give her iron in large doses in order to bring back the color to her cheeks and to restore her strength. For my own part, I follow Niemeyer in allowing my chlorotic patients perfect freedom in their choice of food and the amount of exercise they take, when once I have satisfied myself that they are really suffering from simple chlorosis, and not from symptomatic or idiopathic anæmia; and in the vast majority of cases I find no reason to regret my absolute reliance upon iron. After the chlorosis itself has been cured, and not before, I give directions about food, exercise, and so forth, in order, if possible, to prevent a relapse. For I know that the patient, when once she has got back her appetite and strength, will give herself to the carrying out of my instructions far more willingly than if I had bothered her, while still weak and ill, to do things usually most repugnant to persons in her bodily condition.

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[1] *Niemeyer's* Practical Medicine, translated by Humphreys and Hackley, Vol. II. p. 725.

How is the exceptional efficacy of iron in chlorosis to be accounted for? There is experimental evidence in favor of the belief that iron increases the formation of red corpuscles, or, in other words, of the iron-containing hæmoglobin; and we already know that an oligocythæmia or oligochromæmia is the essential element in chlorosis. From what I said about the use of iron in anæmia (p. 466), the reader may recollect that the metal was specially indicated in proportion as the oligocythæmia predominated over the hypalbuminosis and other associated alterations in the blood. Hence, we might expect iron to be very serviceable in chlorosis, since the blood-change in this malady affects the colored elements alone and with great severity. Conversely, the admirable effect of ferruginous remedies in pure, uncomplicated chlorosis affords the best argument in favor of the above theory concerning their mode of action, and also in support of the view hitherto adopted concerning the nature of the alteration in the blood. For, when the action of a remedy is at once so striking and so constant, it may be adduced as empirical evidence in favor of a theory concerning the mode of action of the remedy in question, as well as of a theory concerning the nature of the morbid process.

Another point in reference to the effect of iron in chlorosis is less easily understood, viz., that large doses of the remedy cure the disease far more certainly and quickly than small ones. Whether large or small doses be given, the quantity of iron actually absorbed is insignificant; this is clear from the black color of the fæces after a considerable dose, due as it is to the formation of insoluble iron sulphide in the bowel. Nevertheless, as Binz justly remarks, the administration of small doses, recommended by some writers on theoretical grounds, has never become popular; and my own very numerous observations have convinced me of the immense superiority of large doses in the treatment of true, uncomplicated chlorosis. I have notes of many cases in which chlorotic patients were treated "rationally" for many weeks with small and "cautiously increased" doses of iron without appreciable benefit, recovering very quickly after I had prescribed the remedy in sufficient quantities. I am so sure of the good effect of iron in large doses that I prefer treating my chlorotic patients at home, to sending them to St. Moritz, Pyrmont, Driburg, etc. For the action of these mineral waters in chlorosis, owing to the relatively small proportion of iron they contain, is far slower and more uncertain than that of pharmaceutical compounds whose strength may be regulated by the prescriber. When the patient's lips and cheeks have regained their color, when she is once more able to enjoy life and movement, I recommend a visit to a watering-place; and I quite believe that the effervescing chalybeate waters just referred to, in combination with the other invigorating conditions of life in a health-resort, may prevent a relapse in cases where a predisposition already exists, and may render that predisposition latent for a considerable length of time.

I have already said all I have to say about the choice of a ferruginous compound (p. 470). I enumerated the more important preparations of iron and briefly analyzed their respective merits and defects. I need only add that I agree with Niemeyer in thinking the dose of more importance than the compound selected. It may be well, however, to choose those preparations which are least likely to impair digestion even in large doses. Accordingly, reduced iron, pyrophosphate of iron, and solutions of the salts of iron with organic acids, are specially worthy of recommendation. At the Basle Hospital, we always treat chlorosis with Blaud's pills, modified in conformity with Niemeyer's suggestions (120 pills instead of the 48 boli recommended by Blaud). And we are so thoroughly satisfied with the effect of these "*pilulae antichloroticae*," of which from 3 to 5 are taken thrice daily, that we have no inducement to vary our treatment of the disease. Whether the singularly prompt and certain action of these pills is to be attributed to their containing potassium as well as iron (both of them entering into the composition of the red blood-corpuscles), is a question that may fairly be asked, but cannot be positively answered.

Although we assign the foremost place among our remedies for chlorosis to iron, and although we treat the disease, from the very first, with iron alone, still it must not be forgotten that this metal only removes the symptoms, leaving the inherent tendency (the congenital hypoplasia of the blood and vascular system) untouched. When this tendency is deeply rooted in the system a relapse is very likely to occur sooner or later after the iron has been discontinued. Such relapses must be treated in exactly the same way as the original attack, and yield quite as readily to treatment, though only for a time.

What I have already stated shows that there is no need to look for any substitute for iron. Attempts to vindicate for other remedies, *e. g.*, manganese, a place in the treatment of chlorosis (Hannon), have all of them been discredited. Attempts to establish the existence of a "manganese chlorosis" in contradistinction to an "iron chlorosis" have completely failed. I need not here stir up such antiquated rubbish; the reader may institute inquiries of his own into the history of therapeutics without my help.

But I must not omit to mention that cases of chlorosis do occur in which iron is temporarily contra-indicated; others, too, in which the iron must be combined with other remedies. It is not any diversity in the nature of the chlorotic process itself that renders it necessary for us to deviate from our usual mode of treatment, but the presence of complications, symptoms, or sequelæ requiring independent consideration. Iron is contra-indicated when the symptoms of true chlorosis coexist with those of gastric catarrh (furred tongue, disagreeable taste in the mouth, complete anorexia, oppression at the epigastrium, and nausea). The immediate administration of iron in a case of this sort would aggravate the gastric symptoms; hence, it is better to begin with some preparation of rhubarb, and to keep the patient on low diet until the tongue is clean. Simple feebleness of the digestive organs (to be distinguished from true dyspepsia by the signs enumerated on p. 467) does not in any way contra-indicate the use of iron; on the contrary, the bold administration of iron is the best mode of strengthening the functional energy of the peptic glands, etc. Accordingly, before we decide against iron, we must take all the symptoms into careful consideration, and only defer the use of the remedy if we feel sure that the mucous lining of the stomach is structurally diseased. The presence of an ulcer in the stomach renders it still less capable of bearing ferruginous compounds than does a state of catarrh. Iron will sensibly aggravate the troubles due to the ulcer, viz., the cardialgia and vomiting. But, as I have already pointed out, gastric ulcer is by no means uncommon as a result of chlorosis (p. 551). On the other hand, simple nervous cardialgia, without ulceration, is relatively common as a symptom of chlorosis, and it is most readily cured, together with the primary disease, by giving iron. Hence, if cardialgia and vomiting make their appearance during an attack of chlorosis, or if a patient of chlorotic aspect comes under medical observation with the symptoms enumerated above, we must take care to exclude the presence of an ulcer before we prescribe iron in the usual routine way, and make a careful examination with this possibility in view. Should there be great tenderness, on pressure, over a circumscribed portion of the epigastrium—should the stomach be intolerant of any kind of food, the presence of an ulcer may be viewed as probable. We must then proceed to employ special treatment (Carlsbad water, nitrate of silver in considerable doses, etc., with an appropriate diet) before prescribing iron. On the other hand, should there be no marked epigastric tenderness, should the cardialgia be more prone to occur when the stomach is empty, we may regard the phenomena as simply nervous. Iron may then be prescribed at once, though tentatively and in small doses. by way of precaution. Lastly, it is clear that febrile complications, if the fever be at all severe, will temporarily contra-indicate the use of iron (p. 468).

Sometimes, again, the *indicatio symptomatica*, or the presence of some definite complication or sequela, may oblige us to combine iron with other remedies. For instance, when the patient exhibits nervous symptoms of a marked kind, and the malady takes on a hysterical character, bromide of potassium or other nervine remedies may be given together with the iron. When choreiform paroxysms occur (as they not unfrequently do), arsenic (four to six drops of Fowler's solution three times a day) may be combined with the iron; I recommend this combination with great confidence, for the muscular unrest of such patients generally yields to arsenic with almost magical rapidity. I cannot, of course, find room to allude to all the possible or even to all the more common varieties and complications of chlorosis one by one. The reader may refer, especially for the treatment of complications, to the corresponding chapters of this Cyclopædia. I ought, perhaps, to say that in chlorosis, as in ordinary anæmia, the patient's diminished power of resistance ought never to be lost sight of. Heroic measures, especially of a lowering kind, are dangerous, owing to the oligocythæmia. As a general rule, the physician ought to turn his attention to the chlorosis itself, apart from its complications; and iron should be prescribed as soon as possible in order to rescue the patient at once from the dangerous predicament in which she finds herself.

Finally, under no circumstances ought ordinary therapeutic precautions to be neglected. The state of the bowels should be carefully watched. Chlorotic subjects usually exhibit a tendency to constipation which is often severe, and may cause great trouble and annoyance. Small doses of a mild aperient water (half a glass to a glass of the excellent Hunyadi Janos water), taken the first thing in the morning, or a cup of St. Germain tea on retiring to bed at night, will usually suffice to meet all requirements, and to insure an adequately copious semi-solid motion in the course of the forenoon.

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Appendix to Chlorosis.

Progressive Pernicious Anæmia.

(*Biermer.*)

[Syn.: Essential Malignant Anæmia. Essential Febrile Anæmia.]

Bibliography.—*F. A. Zenker*, Jahresber. der Gesellschaft für Natur und Heilkunde in Dresden für 1853–57. S. 56.—*The same*, Deutsch. Archiv für klin. Medizin. Bd. XIII. S. 348.—*E. Wagner*, Archiv für physiol. Heilk. 1859. XVIII. 415.—*The same*, Die Fettmetamorphose des Herzfleisches. Leipzig. 1864. S. 148 (especially Cases 138 and 144).—*Gusserow*, Archiv für Gynäkologie. Bd. II. (1871). Heft 2. S. 218.—*Phillips*, Guy's Hospital Reports, 3d Series. Vol. XVIII. p. 159 (1873).—*Biermer*, Correspondenzblatt f. schweizer Aerzte. Jahrgang II. (1872). No. 1.—*Ponfick*, Berlin. klin. Wochenschrift (1873). No. 1. —*Immermann*, Deutsches Archiv f. klin. Med. Bd. XIII. S. 209.—*Perl*, Virchow's Archiv (1873). LIX. S. 93.—*G. Gfroerer*, Memorabilien XIX. 3. S. 116 (1874).[1]

Historical Introduction.

The pathology of anæmic processes has lately been enriched with some interesting cases described by Biermer (1871). Such cases had been noticed and described before, but they excited no special interest, and no definite place was assigned to them in our pathological system. Biermer devised a general term to denote his group of cases; that term—"progressive pernicious anæmia"—appears very suitable in the present state of our knowledge, and I have accordingly retained it.

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[1] Postscript.—After the present article was ready for the press and partly in type, I received a copy of *Schuele's* interesting paper entitled "Contributions to our Knowledge of the Pernicious Forms of Anæmia" (Allgemeine Zeitschrift für Psychiatrie. XXXII. 1). To my great regret, I found myself unable to make any use of the cases of progressive lethal anæmia in some forms of severe brain disease which he records. As regards their etiology, they undoubtedly belong to the class of symptomatic anæmia, and ought, therefore, to have been referred to in the first part of my article (on the Ordinary Forms of Anæmia). As regards their symptoms, on the other hand, they are very like, if not identical with, "progressive pernicious anæmia," and accordingly deserve to occupy an intermediate place of their own. But this hybrid character of *Schuele's* cases made it so peculiarly difficult to refer to them, or to incorporate them at any point in my manuscript, that I determined, however unwillingly, to avoid alluding to them altogether. This foot-note has been introduced in order to direct the reader's attention to the original memoir.

In Biermer's first paper he gave an account of a considerable number (fifteen) of cases of a peculiar, malignant form of anæmia, which had come under his notice at Zürich since the year 1867. The addition he thus made to the vast domain of anæmic processes was an important one, and, by including his cases under a special name, he conferred an independent position on this form of anæmia. But Gusserow was really the first to enrich gynæcological literature with an account of several cases (five) of "extreme anæmia in pregnant women," which were likewise observed at Zürich. Apart from minor differences (*e. g.*, absence of hemorrhagic symptoms in Gusserow's cases), there can be no doubt that the two sets of cases agree in their essential features, viz., in the extreme degree of the anæmia and the remarkable malignity of its course; and it is of considerable importance, for the determination of the causes of the disease in question, that both Gusserow and Biermer wrote at Zürich—the concentration of the observed cases in a relatively small topographical area, like the canton of Zürich, apparently pointing to the existence of some local cause of exceptional intensity. That analogous cases have lately been met with elsewhere is proved, *e. g.*, by a memoir from my own pen, published in 1873, containing a detailed account of two cases of progressive pernicious anæmia that came under my observation at the Basle Hospital; also by a paper of G. Gfroerer's (of Heilbronn), published in 1874, describing a case of extreme fatal anæmia in a pregnant woman, which forms a complete pendant to the cases recorded by Gusserow.

I cannot here enter into the question whether the observations in our older literature of extreme fatal anæmia, associated with hemorrhagic symptoms (malignant purpura)—or of febrile chlorosis, with scorbutic symptoms, running a subacute course towards a fatal issue—or of extreme fatty degeneration of the heart, without valvular disease, in young people, especially young pregnant women—ought to be included under the disease we are now considering. Any detailed analysis of such records would be out of place, as I am not writing a monograph on progressive pernicious anæmia. Suffice it to say that Biermer's disease may very easily be confounded with a variety of other affections which resemble it both clinically and anatomically, *e. g.*, with leukhæmia (myelogenic leukhæmia[1]), or with certain infective diseases running an unusual course (typhus, puerperal fever), or, lastly, with some forms of poisoning (by phosphorus). But there are some cases—*e. g.*, that long ago published in a condensed form by Zenker (1856), and recently completed by an account of the post-mortem examination (1874); also several of those recorded by E. Wagner—which must be viewed as undoubted and highly instructive examples of progressive pernicious anæmia. On the other hand, it is very doubtful whether the case of fatty heart and sudden death, observed by C. Hecker[2] in a woman just after delivery, was really similar to those of Gusserow and Gfroerer, for there is no history of previous anæmia coming on without apparent cause. So, too, as regards Phillips' cases (1873) of death from fatty heart in pregnant and puerperal women, I am unable to decide whether they ought all to be included under the head of progressive pernicious anæmia, for a thorough critical analysis of all the records bearing on this and allied forms of anæmia would far exceed the scope of the present article.

These fragmentary remarks must not be brought to a conclusion without some reference to the papers of Ponfick and Perl (already quoted on p. 358) on the "anæmic form of fatty heart." Their observations and inquiries were not, it is true, immediately related to progressive pernicious anæmia; but they certainly facilitate our comprehension of the symptoms and tissue-changes in this disease. Lastly, I suspect that among the cases examined by Ponfick after death there are a few that would have been recognized during life as examples of progressive pernicious anæmia (in Biermer's sense of the word); although, owing to the want of any detailed account of the symptoms, we are unable to determine how many of the cases belonged to the class of essential anæmia, how many to one of its purely symptomatic forms. For I hold that no doubtful case of extreme and fatal anæmia should be admitted into the present category, unless, after we have thoroughly sifted every possible cause, we remain unable to account, either rationally or empirically, for the progressive course of the anæmic symptoms.

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[1] See my memoir, p. 236.

[2] Monatschrift für Geburtskunde. XXIX. 321.

General Definition of the Disease.

The term "progressive pernicious anæmia" ought to be restricted to those cases of extreme anæmia which tend uninterruptedly towards a fatal issue, notwithstanding appropriate tonic treatment, and for the malignity of whose course and termination no adequate cause can be discovered either in the patient's circumstances or in the previous state of her constitution. The former of these characteristics is included, the latter implied, in the name assigned to the disease. By thus limiting its denotation, we distinguish it at once from ordinary chlorosis, since the latter is neither progressively malignant, nor wholly inaccessible to treatment. From the various forms of idiopathic and symptomatic anæmia, it is chiefly distinguished by the utter obscurity that shrouds its pathogeny and causes. For, although in many forms of anæmia (*e. g.*, the cancerous cachexia) our knowledge of the way in which the blood-change is produced may be very imperfect, still we *do* know that some causal relation invariably exists between the noxa and the alteration in the state of the blood and of the nutritive processes — we are acquainted with the etiology, if not with the pathogeny, of the particular case. But an inquiry into the history of a patient suffering from progressive pernicious anæmia shows either that the usual extrinsic and intrinsic causes of anæmia are absent, or else that the sum of discoverable causes, both predisposing and exciting, is wholly inadequate to account for the malignity of the progressive alteration in the blood, either rationally or empirically. Hence, we are thrown back, entirely or in great measure, on an assumption of "unknown" causes or tendencies, to explain either the pathogeny of the whole disease or of a residue of its phenomena. The mystery, of course, is most perplexing when, as occasionally happens,[1] the patient's history affords no clue whatever to the causation of the malady—when the latter seems to arise spontaneously, only to terminate in death.

There is yet another point of great moment implied in our definition of progressive pernicious anæmia. I must briefly allude to it here, in order to prevent any subsequent misconception. It is clear that if the progress of our etiological knowledge should at any future time enable us to trace the development of a certain proportion of cases of malignant anæmia to agencies whose operation is either rationally or empirically understood, those cases will, *ipso facto*, be withdrawn from the present category, and included among the forms of ordinary symptomatic anæmia. The sole plea for retaining them in their former place would be their similarity, as regards symptoms and prognosis, to progressive pernicious anæmia ; on etiological grounds it would be necessary to detach them from the group. For we could not, of course, assume with any degree of certainty, that the progress of research would enable us to assign the residual cases to known agencies at some future period. Still less ought we, at the present time, when the actual causes of progressive pernicious anæmia are quite unknown, to make any premature efforts to establish its etiological unity and independence. We must use the term suggested by Biermer as a sort of provisional shelter for a multitude of cases, possibly of various origin, and, as I shall hereafter point out, differing to some extent in their symptoms. There they may conveniently abide until some more appropriate place be found for them in an etiological classification. But is one such temporary shelter enough? or must we have several, and if so, how many? To these questions I can give no definite answer. The singular concentration of the cases hitherto observed in the relatively small area of the Canton of Zürich renders it just possible (this is mere hypothesis, devoid of proof) that there may be some endemic, perhaps specific, cause at the root of the cases described by Biermer and Gusserow—for to these cases alone must the hypothesis be provisionally restricted.

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[1] See my paper, *Cases* I. and II.

But, whether progressive anæmia originate invariably from one and the same cause, or whether its peculiar symptoms in all their protean combinations spring now from one, now from another principal root, still we can never exclude the operation of other accessory agencies, both predisposing and exciting; and these agencies admit, notwithstanding our ignorance concerning the true cause of the disease, of being grouped, after a fashion, into an etiological system. The following remarks on the etiology of progressive pernicious anæmia must, therefore, be regarded as a summary of the known, not of the essential, causes of the malady; for we are quite unable, as I have already stated, to say anything about the latter at present.

Etiology.

Progressive pernicious anæmia, like chlorosis, has hitherto een far more frequently met with in persons of the female than f the male sex (Zenker, Biermer, Gusserow). But the relative mmunity of the latter is by no means as great, proportionately, s in chlorosis (Immermann). In either sex, the maximum deree of liability corresponds to the period of maturity—from he age of twenty to that of forty years; it is less marked at uberty, during childhood, and in advanced life. Pregnancy s a powerful predisposing cause (Gusserow, Gfroerer), the alady having broken out in a relatively large proportion of ases after a rapid succession of pregnancies. In other cases, gain, it was preceded by morbid processes of a debilitating ind: repeated hemorrhage (from the uterus, from piles), chronic iarrhœa (Biermer), etc.; or the affected persons had been xposed to privations, had been badly lodged, insufficiently fed, c. Sometimes the disease arose spontaneously, without any iscoverable cause either of an external or an internal kind, in ersons previously healthy. We might, perhaps, be inclined to ew the last-named cases as the only genuine ones; a moment's flection, however, is enough to show that thousands are exposed influences of a debilitating kind, and become affected by idiothic or symptomatic anæmia, without continuing to suffer from residual disorder of a progressive and malignant character after the causal factors have been removed. I must again insist on the complete inefficacy of every kind of treatment, both dietetic and medicinal (all the more striking as a certain number of the recorded cases occurred among the poorer class), as a leading feature of the disease—one which distinguishes it alike from chlorosis and ordinary anæmia. It does away with the possible objection stated above, and puts the essentially peculiar character of the cases in a clear light. This being so, the causes I have enumerated sink into comparative insignificance, their purely *auxiliary* agency being most unambiguously demonstrated.

General Description of the Disease.

Progressive pernicious anæmia usually begins insidiously; its beginnings may be completely masked, when, as occasionally happens, it grows out of some previous disease. Sometimes, however, its invasion is subacute; but this is not so common, and has chiefly been observed in pregnant women. Sooner or later, the patient's friends are struck with the change in her appearance; the skin and visible mucous membranes gradually lose all their natural color, becoming as pale as in the most severe chlorosis or in acute anæmia from hemorrhage. The relative integrity of the patient's nutrition and the absence of wasting—so long as no fever has declared itself and the digestive organs are able to do their work—contrast as markedly with the extreme bloodlessness as they do in chlorosis and anæmia from loss of blood. Many of the patients, indeed, may show signs of imperfect nutrition from the first, owing to their having passed through some antecedent illness, or having lived under unhealthy conditions (Biermer); but their state in this respect undergoes no sensible degree of aggravation during the earlier stages of the progressive pernicious anæmia; it is not until fever sets in that, in conformity with the general rule, the growing anæmia becomes associated with an appreciable marasmus. Still there are cases on record (Immermann)—and they merit special notice—in which, notwithstanding fever, the subcutaneous fat has remained intact till death, and has been demonstrated on the post-mortem table. The peculiar change in the patient's aspect, described above, is soon associated with the other—functional—symptoms of severe anæmia. Palpitation of the heart comes on, and may become very troublesome; any exertion brings on dyspnœa; in short, all the symptoms enumerated under the head of "irritable weakness," in my chapter on Anæmia, make their appearance. To these are gradually added digestive atony, marked irritability of the alimentary canal, and a disposition to secondary dyspepsia; lastly, a state of profound exhaustion, betrayed by the frequent occurrence of severe fainting-fits. The patient gradually sinks in the course of a few weeks or months into an utterly prostrate condition; she cannot leave her bed, and any attempt to assume an erect posture exposes her to the risk of fatal syncope. In this state of prostration, absolutely devoid of color, unable to raise herself up, still stirring occasionally, but hardly able to speak above her breath, the patient offers a singular and melancholy spectacle, reminding the onlooker of a corpse continuing to vegetate feebly after death. About this period, sometimes even earlier, signs of moderate dropsy may usually be noticed; the legs may be puffy, there may be signs of effusion into the pericardium and pleural cavities—phenomena which, together with the extreme paleness of the complexion, may suggest kidney-disease and albuminuria. None the less is the urine free from any trace of albumen; even if, as sometimes happens, faint opalescence be caused by heat and nitric acid, a moment's reflection shows that the trace of albumen present cannot account for the gravity of the symptoms, or connect them with a primary affection of the kidneys. A careful examination of the liver, spleen, and lymphatic glands shows that their condition is as inadequate as that of the kidneys, to account for the destructive changes going on in the blood and the steadily increasing prostration. Again, the skin shows none of the bronzing peculiar to Addison's disease, so that we cannot refer the severe constitutional disturbance to disease of the adrenals. Lastly, microscopical examination of the blood throws no light upon the symptoms, affords no evidence of any familiar alteration (leukhæmia, melanæmia, etc.). In a great majority of the cases hitherto observed (Gusserow, Biermer, Immermann), no disproportion in the relative number of red corpuscles and leucocytes has been found to exist. This is enough, especially when taken together with the absence of any enlargement of the spleen, or generalized overgrowth of the lymphatic glands, to distinguish the pure, uncomplicated form of progressive pernicious anæmia from those forms of leukhæmia which clinically resemble it. Even were we to discover some degree of actual leucocytosis in a few cases, we should not, therefore, be justified in regarding the latter as "less simple" forms of the disease, as hybrids between leukhæmia and progressive pernicious anæmia; still less, in classing them summarily under leukhæmia (cf. my subsequent remarks on this point in the sections on Anatomy and Diagnosis).

Among the physical signs of progressive pernicious anæmia (apart from the obvious change of complexion) the most common are certain auscultatory phenomena in the heart and vascular system. Though not in any way pathognomonic, since they are common enough in ordinary anæmia and in chlorosis, they appear to be especially constant and intense in progressive pernicious anæmia, and are therefore entitled to a place among its most characteristic symptoms. A loud, blowing, systolic murmur may nearly always be heard over the heart, both at its apex and especially at its base; it is so loud when the patient is lying down as to suggest the possibility of some organic lesion of the valves. This idea is further confirmed by the frequent existence of a distinct purring tremor (*frémissement cataire*) felt over the præcordia—a tremor such as is not ordinarily perceived save in connection with well-marked valvular mischief. None the less, however, is the presence of organic disease negatived both by the results of examination after death and also during life by the absence of other physical signs, especially those of compensatory hypertrophy. As a rule, the area of præcordial dullness (apart from hydropericardium) is not at all, or at any rate not sensibly increased; the apex-beat is not appreciably displaced outward or downward; the heart's impulse is weak, often wavy and intermittent. In short, the physical signs agree with post-mortem evidence in proving that the heart is either of normal size or moderately dilated, but not hypertrophied. Similar phenomena, though less constant and usually less intense, are also met with in severe anæmia and in chlorosis; by keeping this in mind we shall not fail to interpret the murmurs aright, and shall escape the error of attributing them to valvular imperfection. They must be viewed as accidental or anæmic murmurs, due to functional inadequacy of the *musculi papillares* of both ventricles (cf. p. 399), and indirectly to the altered composition of the blood. Lastly, to make the list of physical signs exactly the same as in typical anæmia, a loud venous hum (with palpable thrill) may usually be detected in the jugular veins. I have already explained the laws by which its intensity is regulated in different cases (p. 400).

The physical signs I have just enumerated must be included, on account of their intensity and constancy, among the essential characters of progressive pernicious anæmia. The bleedings that are frequently associated with them are less constantly observed; when present, however, they are eminently striking and significant. Though more common, as a rule, towards the close of life, they sometimes make their appearance at an early stage, their unexpected outbreak being occasionally the first warning the physician gets of the serious nature of the disease. Should the hemorrhage be abundant and difficult to check, or should it recur at brief intervals from various parts of the body, it may easily hasten the fatal issue by exhausting the patient's strength; but the bleedings are never twice alike in amount or frequency. The anatomical seat of the extravasation is, upon the whole, more constant, though even this may differ widely in different cases, now one part, now another, presenting itself as a *locus minoris resistentiæ*. Epistaxis is perhaps the most common form of hemorrhage; bleeding from the gums, and in women from the genital organs, is also not infrequent; petechiæ have sometimes been observed, and occasionally large patches of ecchymosis. Of those internal hemorrhages that allow of being recognized during life, those into the retina are of peculiar clinical interest, for they are, according to Biermer, among the most constant phenomena of the disease. They may be present in great numbers in both eyes (our observations at the Basle hospital tend to corroborate this statement); on ophthalmoscopic examination, which should never be omitted in doubtful cases, they appear either as small, black, reddish or yellowish brown spots, or as larger dark patches or clouds of irregular outline which veil a great part of the fundus, or, lastly, as ecchymotic striæ radiating from the centre of the optic disk. When very minute, these extravasations may be present in great number without causing any disturbance of vision ; on the other hand, solitary hemorrhages of larger dimensions give rise to sensible dimness of vision (and that very suddenly), to circumscribed obscuration of the visual field, etc. For example, a patient suffering from progressive pernicious anæmia in an early stage, who had not been undergoing any treatment, came to seek advice at the Basle hospital for sudden loss of sight in one eye ; he was thus introduced to our notice as it were by an accident. Besides these visible extravasations, others not unfrequently occur into internal parts, and give rise to symptoms varying in their gravity and nature according to the seat of hemorrhage and the amount of blood effused. Such bleedings may even prove the immediate cause of death. Thus, *e. g.*, in one of Biermer's cases the patient succumbed quite unexpectedly to apoplexy resulting from extensive cerebral hemorrhage and breaking down of brain tissue. Numerous capillary extravasations have occasionally been found in the brain after death, without their presence having been betrayed by symptoms during life.

Another and a more important symptom of progressive pernicious anæmia is fever. This was present in both my cases, and in almost all of those recorded by Biermer. It is noteworthy that the febrile movement usually sets in as life is drawing to a close, and does not precede the development of the anæmia ; now and then, however, it comes on earlier, but it is never the *first* symptom. The fever is of a wholly irregular type ; it is generally moderate and of the continued kind, but its continuity is broken by occasional temporary exacerbations (when the temperature may run up to 40° C. = 104° F.) and remissions during its daily course. Taken as a whole, the temperature curve usually exhibits a relapsing character, the continuous pyrexial periods—lasting for days or even weeks—being separated by shorter or longer apyretic intervals. Lastly, the temperature is prone to fall suddenly as the end approaches, death sometimes taking place when the heat of the body has been reduced to an extraordinarily low point (35° C. or even 34° C., 95° F. or even 93.2° F.), after having kept at a febrile, or, at any rate, sub-febrile level during the proagonic period. I may add that the regular symptoms of fever—anorexia, furred tongue, thirst, heat of skin, and even shivering—are usually present in this anæmic variety of fever when its paroxysms are at all severe. When they are mild, however, the enfeebled and bedridden patient may be unconscious of their presence, which is only revealed by the use of the thermometer. Such differences of subjective appreciation are not, of course, in any way peculiar to the disease we are considering. Concerning the elimination of urea and carbonic acid in this form of fever we possess no information.

Such are the only distinctive characters exhibited by progressive pernicious anæmia. Its other symptoms are just like those of ordinary symptomatic anæmia, from which they differ mainly in their unusual intensity, the absence of any considerable degree of marasmus and of any such coarse lesions as might suffice to account for the severe and fatal alteration in the blood. When the disease becomes developed in a pregnant woman, pregnancy does not usually go on to its full term, premature labor generally setting in during the eighth month (Gusserow) after the symptoms of the disease have reached their point of culmination. So far as our present experience goes, this event must be regarded as the immediate forerunner of death, the patients never having survived delivery for more than a few hours. No special cause for the premature occurrence of uterine contraction could be made out; it seemed almost as though the fatal intensity of the anæmia had itself played the part of an oxytocic, and provoked the expulsion of the contents of the womb.

Anatomical Alterations.

Rigor mortis is usually slight and late in making its appearance, after death from progressive pernicious anæmia. The body not unfrequently appears rather badly nourished; still, if we take its condition before the onset of the disease as our standard of comparison, we shall generally be struck with the trifling amount of emaciation that has occurred. Where the patient was originally of stout habit, the body will appear plump and the *panniculus* loaded with fat. Some œdema may nearly always be detected in the lower extremities ; often, too, in the face, on the backs of the hands, and in the soft coverings of the trunk. The œdematous parts are, of course, increased in bulk, and any signs of wasting obliterated. Even before the body is opened, the extreme paleness of the skin (such as is only seen in persons who have bled to death), and the absence of hypostatic staining, attract attention. While the signs of hypostatic congestion, such as are hardly ever absent in bodies containing a fair amount of blood, are almost entirely wanting, there may be a more or less abundant crop of petechiæ scattered over the trunk and limbs. These are generally minute (no bigger than a lentil), of a bluish purple, greenish blue, or yellowish brown tint. Larger ecchymoses of irregular outline are also met with now and then ; they exhibit the various shades of color characteristic of extravasated hæmoglobin. Lastly, there may be vibices, *i. e.*, striped extravasations into the skin, much longer than they are broad. These are usually produced on parts exposed to linear pressure during life by creases in the bed-linen, etc. Hence, they are most common about the shoulders, neck, loins, and trochanteric regions.

A considerable amount of clear fluid usually escapes from the great cavities (thorax, pericardium, abdomen, skull) of the body when they are opened. Sometimes the fluid is bloody, as in the abdomen of Zenker's case. Extravasations, varying in size and number, have also been met with in many other internal parts, *e. g.*, in the brain (Biermer, Zenker), in the naso-pharyngeal cavity, on the visceral layer of the pericardium (Zenker), in the vagina and ovaries (Zenker). I have already said enough about the relative frequency of hemorrhage into the retina, which may be recognized during life with the ophthalmoscope ; I need only add that inflammatory cloudiness of the retina (purulent retinitis) such as has occasionally been observed in conjunction with simple extravasations in leukhæmic patients, has not hitherto been met with in progressive pernicious anæmia.

The internal viscera, like the skin, are pale and bloodless.

Hence, the special tint of every organ is extremely vivid, just as in persons who have bled to death (p. 355). No trace of injury or serious local disease can be detected; nowhere can we find any malignant growth, such as might explain the extreme and universal bloodlessness. The spleen, the lymphatic glands, the marrow of the bones (Ponfick), show no sign of hyperplastic activity or of anything abnormal beyond extreme paleness. The kidneys, besides being anæmic, sometimes exhibit commencing fatty change in their epithelial elements; but never any inflammatory swelling of their cortical substance, nor yet advanced degeneration; sometimes, though absolutely bloodless, they are otherwise quite normal. The same is true of the liver, the gastric glands, and most of the remaining viscera; apart from their extreme bloodlessness, they are wholly free from any coarse changes, though they may occasionally show signs, more or less decided, of fatty degeneration.

The tissue-changes in the heart and vascular system are similar in kind to those just described in other organs, but they are more constant and more severe. The heart, of normal size or somewhat dilated, always shows traces of fatty change (p. 382) in its muscular fibre, either in the form of diffuse yellowish discoloration (when the degenerative changes are moderate in degree), or in that of circumscribed patches, dots, and striæ of an intensely yellow tint. In this, as in the more ordinary forms of anæmia, the change is always most intense in the *musculi papillares;* but the rest of the heart does not always escape, and may, in well-marked cases of the disease, appear universally speckled (Zenker). These important alterations in the muscular tissue contrast forcibly with the integrity of all the valves and orifices; and the contrast throws light on the true origin of the murmurs, proving that they depend on disease of the muscle, not on any lesion of the valves due to endocarditis, whose existence may have been erroneously suspected during life. The habitual integrity of the valves does not, of course, exclude the occasional presence of traces of fatty degeneration in their tissue, similar traces being very commonly met with in other parts of the vascular system. Thus, for instance, we almost always find them in the inner coat of the larger arteries, especially the aorta and its primary divisions; moreover, Biermer has observed fatty degeneration of certain capillary tracts, especially in the brain. Considering the intimate histological relationship that undoubtedly subsists between chlorosis and progressive pernicious anæmia, and which occasionally extends to their etiology and course (cf. section on Complications), it is worthy of note that in a few cases of progressive pernicious anæmia the arterial system has been found abnormally narrow—a state of things precisely analogous to the chlorotic hypoplasia of the vascular apparatus having been demonstrated on the post-mortem table (Zenker). In other cases no such anomaly of development has been noticed, or the aorta and its main branches are stated to have been of normal calibre and their walls of normal thickness and elasticity (Immermann).

The extreme and universal paleness of all parts of the body may be accounted for by an oligocythæmia or oligæmia of exceptional intensity. This view is further corroborated by the state of the blood in the cavities of the heart and in the great venous trunks. The blood contained in the heart is unusually pale in color; its quantity is very small, so that the heart and the great veins, like the remainder of the vascular system, are sometimes found nearly empty; finally, it is very watery, and shows little disposition to coagulate, sometimes remaining in a perfectly fluid condition after death. In other cases a few clots may be found amid the fluid blood, but they are of loose consistency and easily torn. Taken in conjunction with the extreme and universal decoloration and the signs of dropsy, these characters presented by the blood, after death from progressive pernicious anæmia, point to the existence not only of oligæmia (diminished volume of the blood) and oligocythæmia (diminished number of red corpuscles), but also of a certain degree of hypalbuminosis and of hypinosis (deficiency of fibrin). Accordingly, the blood-change in this disease is far more serious and complex than in chlorosis, even though, in both cases, an extreme oligocythæmia appears to be the most important of the fundamental alterations in the blood. The proportion of red to colorless corpuscles seems to vary in different cases. While, as I stated above, microscopical examination of the blood in a majority of the patients during life showed no abnormal relation between the number of the two kinds of elements, Ponfick discovered a well-marked degree of *relative* leucocytosis in a case of progressive pernicious anæmia with fatty heart (a case undoubtedly belonging to the category established by Biermer), which he had an opportunity of dissecting after death. The pale red, perfectly fluid blood taken from the dead body showed no trace of fibrinous coagula, even after it had been allowed to stand for some time in a test-tube; it behaved just like normal blood mixed with some substance that prevents coagulation. Its constituent elements gradually distributed themselves in horizontal layers according to their relative gravity; and the extreme diminution in the number of red corpuscles was then unmistakably displayed, the lowest (heaviest) stratum being scarcely at all thicker than the superjacent layer of leucocytes. Hence, the number of leucocytes appeared much increased in proportion to that of red corpuscles; while, at the same time, the actual depth of the stratum of leucocytes proved that no *absolute* increase in their number had occurred. Moreover, the absence of any signs of overgrowth in the spleen, lymphatic glands, and medulla of the bones, effectually set aside all possibility of the presence of leukhæmia. Still, this case shows that microscopical examination of the blood in progressive pernicious anæmia during life (p. 579) may occasionally yield results exactly similar to those obtained by the examination of the blood in true leukhæmia, viz., an increase in the proportion of colorless elements, though *relative* instead of being *absolute*. And yet, as I have just shown, the similarity between the cases is only apparent; there is no leukhæmic change, not even a combination of leukhæmia with progressive pernicious anæmia, but only a peculiar modification of the latter disease, in which the number of red corpuscles is diminished in an enormously greater proportion than the number of colorless ones. As a general rule, there will be no difficulty in distinguishing this variety of Biermer's disease from true leukhæmia, especially if the normal condition of the spleen and lymphatic glands (whether in the living or the dead body) be taken into account. Still, as I shall have to point out subsequently, cases do occur in which the diagnosis is surrounded by very great difficulties.

Special Symptomatology.

Analysis of the Symptoms and Post-mortem Appearances.

A reference to the two preceding chapters (Anæmia and Chlorosis) is enough to show that an overwhelming majority of all the symptoms of progressive anæmia are identical *in kind* with those presented by ordinary anæmia of a severe type and by intense chlorosis. As I have already analyzed every one of these symptoms very fully, both from the physiological and the pathological side, I need hardly go over the same ground again. Accordingly, I will pass over the decoloration of the skin and mucous membranes, the dropsy, the functional enfeeblement of all parts of the body (especially the heart and voluntary muscles), and the auscultatory phenomena presented by the vascular apparatus. When once we have realized that a very extreme degree of anæmia or oligocythæmia forms the pathological groundwork of the disease, we are able to deduce nearly all its characters from the blood-change as simple and inevitable consequences; and the exceptional intensity displayed by those characters is fully explained by the exceptional intensity of the spanæmia. Those morbid changes—such as fatty degeneration of the heart and other tissues, hemorrhage from the mucous surfaces and into the skin, retina, etc.—which are at once of greater pathological interest and more palpable than the disorders of function, may be explained in the same way. I have already said enough (p. 356) about the fatty change that occurs in various tissues, especially in the heart, in Biermer's anæmia, to show that it is in no sense to be regarded as specific. If we bear in mind that this necrobiotic change occurs in all forms of anæmia, provided they are sufficiently severe and involve extreme oligocythæmia, we shall not be surprised to find the excessive diminution in the number of red corpuscles, which is so constant a feature of progressive pernicious anæmia, associated with a considerable degree of fatty degeneration in the heart and elsewhere. The same may be said of the hemorrhagic phenomena; they are not in any way pathognomonic of Biermer's anæmia, but are likewise met with—as epistaxis, petechiæ, and even retinal extravasations—in certain other forms of anæmia and allied processes. It is particularly instructive to compare simple pernicious anæmia in this respect with so-called pseudo-leukhæmia (*anæmia splenica et lymphatica*), and also with true leukhæmia; the tendency to hemorrhage being as marked in these two diseases as in Biermer's anæmia. If we go on to inquire what histological character the leukhæmic and pseudo-leukhæmic processes have in common with progressive pernicious anæmia, whose singular clinical malignity they share, we find, in the first place, that it does *not* consist in hyperplastic enlargement of the spleen, lymphatic glands, etc., *nor*, secondly, in an increase of the number of leucocytes in the blood, *but*, solely and entirely, in an excessive diminution in the number of red disks, which is equally striking in all three diseases. It is, accordingly, this *oligocythæmia rubra* (which is hardly ever met with, in the same monstrous proportions, under any other circumstances) which must be regarded as the essential cause of the hemorrhagic diathesis in progressive pernicious anæmia, as well as in leukhæmia and pseudo-leukhæmia. The first of these three diseases appears to furnish the simplest, and therefore most instructive clinical proof of this assertion, for the histological conditions associated with it are obviously less complex than those in the remaining two. In my opinion (and I believe it to be in harmony with the results of experimental research) the normal renewal of the capillary walls—whether functional or nutritive—demands that they shall be in contact with highly oxygenated blood. When the supply of such blood runs short, structural changes, slight at first, and subsequently coarser (fatty degeneration), become developed in the capillary walls, and allow extravasation to take place, at first *per diapedesin*, and afterwards *per rhexin* also. As in Cohnheim's well-known experiments "on the dependence of the integrity of the vascular walls upon the circulation,"[1] a temporary arrest of the blood-supply to a limited vascular area causes a complete, though transient, interruption in the supply of oxygen to that area, so a like effect is produced upon the entire vascular system, in a more lasting though at the same time less absolute fashion, when the number of oxygen-carriers in the blood is excessively reduced. By regarding this as the true connection between the hemorrhagic diathesis on the one hand, and the oligocythæmia on the other, we can readily understand, not merely why the tendency to bleed should be so exceptionally pronounced in the three diseases we have been comparing with one another, but also why it should be so much less common in other forms of anæmia, and especially in chlorosis. In severe cases of the last-named affection, the numerical diminution of the red corpuscles is indeed extreme; but it hardly ever reaches that degree which is obviously necessary if it is, alone and directly, to produce the hemorrhagic diathesis. Of course, I quite admit that this diathesis may be, and perhaps often is, produced by other causes. Indeed, I firmly believe that some such accessory causes must be in operation whenever we find hemorrhagic symptoms developed in connection with a moderate degree of oligocythæmia, or even without any oligocythæmia at all. (See the observations on this subject in the chapters on Scurvy, Hæmophilia, and Purpura.)

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[1] Untersuchungen über die embolischen Prozesse. Berlin, 1872, p. 28–57.

In the most severe forms of chlorosis, the red corpuscles (or the hæmoglobin of the blood) may, as I have already pointed out (p. 526), undergo a maximum reduction amounting to from fifty to seventy-five per cent. of their normal number. That in well-marked leukhæmia, on the other hand, the diminution in the number of red corpuscles is far greater, seems highly probable, for we have reason to believe that in leukhæmia the *oligocythæmia rubra* is essentially due to a failure on the part of the rudimentary corpuscles to develop at the right moment into colored disks; instead of doing this, they degenerate, for the most part, into leucocytes. Hence, we are able approximately (though by no means accurately) to measure the absolute reduction in the number of red corpuscles by the increase in the proportion of leucocytes in the blood. Now, we know that in leukhæmia the colorless may be nearly or quite equal in number to the colored elements; this would indicate a most enormous reduction in the latter, since, under normal conditions, we find only one leucocyte to about three hundred red disks. True, we are not justified in concluding that the diminution in the number of red corpuscles is precisely equivalent to the increase in the number of colorless ones; it may be that in leukhæmia the total number of corpuscular elements in the blood is augmented (*sc.*, the sum of red + colorless elements) by a disproportionate increase in the number of leucocytes without a corresponding diminution in the number of red corpuscles. Still, in the final stage of leukhæmia, when (just as in pseudo-leukhæmia and progressive pernicious anæmia) the hemorrhagic symptoms are most conspicuous, the total number of colored elements in the blood must amount to a very small fraction indeed of their original number during health. Besides, Zenker showed long ago that the hemorrhagic tendency in leukhæmia could not be attributed to the augmentation in the number of leucocytes; he pointed out that hemorrhages of an exactly similar kind might occur, without any leucocytosis, in those peculiar maladies which we nowadays include either under pseudo-leukhæmia or under progressive anæmia—such cases having been occasionally observed even at the time when Zenker wrote, though they had not yet received any special names or places in our systematic pathology.

There still remains one symptom of progressive pernicious anæmia to be considered, whose constant presence renders it one of the most noteworthy characteristics of the disease, while at the same time it is singularly difficult of explanation under the pathological conditions that are here associated with it. I mean fever. In my own cases, as in those of Biermer, no adequate local cause for the pyrexia could be discovered. Hence, I am obliged, like Biermer, to refer it to a humoral origin, *i. e.*, to bring it into immediate causal connection with the anæmic state of the blood. Provisionally, therefore, I am willing to employ the term "anæmic fever," chosen by Biermer. But how can an anæmic condition of the blood, specially characterized by a diminution in the amount of oxygen-carrying hæmoglobin, be made to account for fever? We know that, as a general rule, it lowers the temperature of the body (p. 378). We are, unfortunately, unable to furnish any exhaustive answer to this puzzling question, since, owing to the novelty of the facts themselves, and the small number of cases observed, no direct investigations have hitherto been made into the causes and mode of origin of "anæmic fever." I must be content to suggest a few possibilities which ought to be kept in mind, and which may, perhaps, turn out hereafter to be important in reference to the pathogeny and etiology of this peculiar form of pyrexia. These suggestions will not commit us to any positive theory concerning its nature; they may serve, however, to mark out the limits within which future inquiries into the subject will have to be conducted.

In the first place, we are not justified in attempting to invert the causal relation between the anæmia and the fever, and to ascribe the malignant impoverishment of the blood wholly, or even principally, to the fever. The following are the reasons against any such attempt: (1.) The anæmia is too extreme in degree to be accounted for by either the intensity or the duration of the fever. (2.) The febrile movement does not usually set in till after the anæmia has already made some progress. The belief that the fever cannot possibly be the unknown prime cause of the malignant anæmia is quite compatible with a recognition of the fact that the fever usually hastens the course of a progressive anæmia which has hitherto been unattended with any rise of temperature. The fever becomes an auxiliary factor in bringing about the final catastrophe, though it has nothing to do with the initial processes of the disease. The only hypotheses still open to us are, either that both fever and anæmia are joint effects of some one fundamental cause, or that the excessive anæmia is itself the immediate cause of the fever. The former view will obviously gain in probability if it should be proved that many or all cases of progressive pernicious anæmia are due to the operation of certain hitherto unknown specific noxæ of an infective character. We might then suppose that some decomposition of the plasmatic albuminates, the red corpuscles, etc.—some zymotic phenomena attended by a production of heat—takes place in the blood itself; the increase of heat production occasionally manifesting itself by a febrile rise of temperature, and in any case by the development of a progressive anæmia. So long, however, as no direct evidence of the existence of a specific cause has been obtained —so long as it continues to be doubtful whether progressive pernicious anæmia is always due to the same cause (p. 576)—we shall be on the safe side in recognizing the possible truth of our remaining hypothesis, viz., that the fever may be a direct result of the extreme anæmia. That this view is not necessarily an absurd one— that it is not without support from clinical analogy—is evident if we take leukhæmia and pseudo-leukhæmia, two morbid processes which have many points of contact with progressive anæmia, into consideration. These two diseases are almost always attended by fever; the febrile symptoms making their appearance, just as in simple pernicious anæmia, towards the close of the disease—*i. e.*, at a time when the splenic tumor, enlargement of the lymphatic glands, etc., are already present, and the consecutive blood-change has attained its maximum degree of development. Hence, there are grounds for seeking the cause of the pyrexia, in these affections likewise, not so much in the hyperplastic changes that occur in the cytogenic organs, but in the altered composition of the blood itself; all the more as the very same febrile movement occurs in progressive anæmia *without* any previous or subsequent enlargement of the spleen, lymphatic glands, etc. A chain of reasoning, analogous to that given above, will ultimately bring us to the hypothesis that the probable cause of the anæmic, leukhæmic, and pseudo-leukhæmic fever must be looked for in the excessive *oligocythæmia rubra*. Put into more general, and therefore more correct language, the hypothesis may be formulated thus: the aggregate of symptoms constituting fever may and habitually does arise whenever the total number of red corpuscles is reduced, from any cause, below a certain—always very low—proportion; always supposing the patient to survive for a sufficient time. I quite admit, for my own part, that I am disposed to regard this hypothesis as the true one, though of course I do not consider it proved. Some further data of an empiri-

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cal kind may, however, be urged in its favor. In the first place, I shall refer to some facts that have been observed in men and animals bled from a vein. As Frese has shown (Virchow's Archiv, XL. 303), a large venesection is followed by a considerable fall of temperature; but this is momentary, and is succeeded by a rise which considerably exceeds the normal level before the venesection, and may attain a febrile height. So, too, it was found by J. Bauer (p. 376) that the production of urea is temporarily increased by bleeding, and that artificially induced spanæmia is clearly followed by increased decomposition of "organ-albumen." Again, in speaking of chlorosis, I alluded incidentally to the occasional occurrence of transient febrile symptoms in exceptionally severe cases of this disease; febrile symptoms unattended by any other palpable alterations (Wunderlich, Schulz, and others). Lastly, I may refer to the well-known fact that excessively anæmic convalescents present a singular instability of temperature, and are very liable to suffer from febrile paroxysms without apparent cause. These facts all tend to show that extreme anæmia is in some way connected with a tendency to febrile symptoms which may, under certain conditions, pass into actual fever.

It may be asked how we are to imagine the rise of temperature to be connected with the oligocythæmia? Supposing a causal relation really to exist between them, the pyrogenic element must obviously consist (as in any other form of fever) either in diminished loss or in augmented production of heat, or in a combination of the two. Inasmuch as, at the present time, the ordinary forms of pyrexia are usually and in all likelihood rightly attributed to the combined influence of retention and production, we may fairly assume that they jointly contribute to produce "anæmic fever." In order to carry out this idea we should have to suppose, in the first place, that the altered blood—the dyscrasia—acts as an irritant on the peripheral vaso-motor nerves, causing a periodic ischæmia, varying in degree, of the surface of the body. In conformity with simple physical laws, this would give rise to an alternate retention and escape of heat, *i. e.* (supposing heat production to go on at a uniform rate), to alternate elevation and depression of temperature. But there is nothing absurd—though it may appear at first sight paradoxical—in believing the production of heat to be increased likewise, even when the blood is very poor in oxygen; nay, Bauer's observation that an increased elimination of urea is among the consequences of a copious venesection, is decidedly in favor of the idea hat certain chemical processes, attended by an evolution of heat, are rendered more ctive than usual. It must not be forgotten that the activity of the molecular hanges and of heat production in the living cell is not necessarily proportionate o the store of energy actually present in the blood. Under ordinary circumstances, ndeed, a proportion of this sort *is* maintained, the actual energy employed in issue-metabolism being derived from the potential energy contained in the funcionally active constituents of the blood; the latter undergoing conversion (p. 379), n the interior of the living cell, into external molecular work (heat, motion, electriity, etc.). The better, accordingly, the composition of the blood, the more favorble, *cæteris paribus*, will be the conditions essential to nutrition and the production f heat. But even under normal circumstances the intensity of these processes does not depend *exclusively* upon the quantity of the blood; the tissue elements themselves, according to their specific nature and varying state, doing their work now slower, now quicker, the condition of the blood remaining constant, *i. e.*, they may withdraw a varying proportion of material charged with potential energy from the blood in a unit of time, and they may further convert a variable fraction of this potential energy into actual work. Accordingly, even when the anæmia, and especially the oligocythæmia, are very considerable in degree, an abnormal amount of heat may be generated whenever the nutritive excitement of the tissue-elements happens for any reason to be greatly increased. But there is not the smallest ground for thinking that any such increase takes place in progressive pernicious anæmia, leukhæmia, etc., and hence it does not seem justifiable, at any rate with our present knowledge, to ascribe the "anæmic fever" to a hypothetical exaltation of trophic energy in the tissue-elements, provoked by the extreme oligocythæmia. There is another and more likely way of looking at the matter; the extremely inadequate composition of the nutrient fluid—more especially the extreme reduction in the number of red corpuscles—in progressive anæmia and allied disorders may be supposed to cause, not an increased activity of nutrition (clearly a most improbable hypothesis), but a spontaneous decay or necrobiosis of innumerable tissue-elements. This view is supported by the anatomical changes in the muscular substance of the heart, etc. There is nothing absurd in supposing that the molecular structure of the cell is, from a chemical point of view, lax and unstable, requiring (at any rate in the more highly organized animals) a continual restorative activity on the part of the blood for its maintenance. Should this restorative influence fail or prove inadequate, owing to some defect in the composition of the nutrient fluid, the complex substance of which the cell consists will spontaneously decay and break up into a number of more stable products. But we know that heat is always set free when chemical compounds of a more stable kind are generated from such as are less stable, even when oxidation has no part in the process. Thus we have a possible source of increased heat-production in those extreme forms of blood-disease of which progressive pernicious anæmia is the chief type, and by combining its influence with that of heat-retention we may construct a possible theory which will account for the "anæmic fever." Further observation and direct experiment will be required to show whether the above speculations correspond to the reality or not.

Nature and Pathogeny of the Disease.

It is clear that the essential nature of these enigmatical cases of pernicious anæmia will remain a mystery until we have ascertained the ultimate and hitherto unknown causes of the disease. But our ignorance of them need not prevent us from inquiring into its pathogeny; for the latter, at any rate in its more general features, admits of being deduced from the symptoms in many diseases whose causation is obscure. In this, as in all other forms of anæmia, there are only three possibilities among which we have to choose (p. 291): the anæmia may be primarily due to inanition, or to consumption, or to both together. But even these elementary questions must, for the present, remain unanswered; we neither know in which of these three possible modes progressive pernicious anæmia comes about, nor even whether its mode of origin is the same in all cases. It is quite possible that both in their pathogeny and in their etiology different cases may differ widely from one another. Great as is the likeness (apart from the final issue) between progressive pernicious anæmia and severe chlorosis—much as we may be disposed to regard an arrest of sanguification, an inanition of the blood, as the principal factor in the former disease, nevertheless, the occurrence of febrile symptoms (so far as they are not a direct consequence of the anæmia) renders it possible that the malignant impoverishment of the blood may be due primarily to consumption, or even to the combined influence of consumption and inanition. Precise investigations concerning tissue-metabolism—concerning the production of urea and carbonic acid—before and during the anæmic fever, will undoubtedly shed light on these points at some future time. Our present dearth of information on this subject must be ascribed partly to the rare occurrence of the disease, partly to the fact that the importance of getting an answer to these questions has not hitherto been recognized, and no adequate clinical investigations have accordingly been undertaken.

Complications and Sequelæ.

In speaking of the causes of progressive pernicious anæmia, I pointed out that it not unfrequently breaks out in persons exposed to various debilitating influences (unhealthy dwellings, want of food, exhausting discharges, etc.); but that no such influences can be regarded as the cardinal elements in its causation. Perhaps it may be more correct to speak of the pernicious anæmia in such cases as a complication supervening on an ordinary idiopathic or symptomatic anæmia, the true causes of the complication being totally unknown. Moreover, I am inclined to put the same interpretation on those cases of chlorosis in which, after the usual symptoms have lasted for a variable time and the diagnosis has been correctly established, fever comes on without any obvious cause, hemorrhagic accidents are developed, and the patient succumbs at the end of a few weeks, in a state of utter prostration, and in spite of the most vigorous tonic treatment (Wunderlich). For, if we compare the course of the malady in such exceptional cases with that which it ordinarily follows, we can hardly avoid the conclusion that the disease was at first a simple chlorosis, which may possibly have retained its uncomplicated form for some considerable length of time, and that, at a given moment, certain fresh causes of an unknown order came into operation and modified the usual symptoms of chlorosis so as to make the disease assume the character of a pernicious anæmia. In formal language, we are driven to assert that the malignant constitutional disorder has supervened, in consequence of unknown causes, upon an ordinary chlorosis as a complication or sequela of the latter. Whether the pernicious anæmia grow out of a chlorosis or a common anæmia, it is the malignity of the disease, the absence of any sufficient cause for this malignity, and the addition of certain special characteristics (fever, hemorrhagic diathesis) that throw up the complication from the background of the antecedent and more ordinary affection, and entitle it to claim the rank of an independent process. And if it is to have a name of its own, that chosen by Biermer seems for the present to be the most appropriate one; for the state we are now considering is clinically identical with that "progressive pernicious anæmia" which, as we have already learned, may arise without any pathological antecedents, and without any known cause ("spontaneously"), in previously healthy persons (p. 575).

But in the above cases, we have been considering, not any complications or sequelæ of progressive pernicious anæmia, but the latter disease as itself a terminal complication of other maladies (of anæmia or of chlorosis). We have next to inquire whether, in the course of a progressive pernicious anæmia, any further complications may arise? Apart from certain catastrophic phenomena, *e. g.*, cerebral hemorrhage (Biermer), which are occasionally met with, but which, strictly speaking, ought to be viewed as symptoms, or as peculiarly unfortunate localizations of the general hemorrhagic diathesis, etc., we cannot be said to know of any. Progressive pernicious anæmia, looked at from a clinical point of view, occurs either as an independent malady, or as the closing member of a series of constitutional disturbances—as the direct cause of the lethal issue, by leading to a gradual extinction of all the organic functions.

Diagnosis.

We may suspect the presence of progressive pernicious anæmia whenever we find the symptoms of ordinary anæmia, especially the pallor of the integument and the failure of bodily energy, developed in an extreme degree without there being any discoverable organic disease to account for their intensity. Our suspicions will be strengthened if the patient is of the female sex and if the illness has come on during pregnancy; for we know that pernicious anæmia is most common in pregnant women. But in these very cases we must be extremely careful to examine the urine, for a similar degree of paleness and debility may result from serious kidney-disease with albuminuria becoming imperceptibly developed during gestation. When intense anæmia, apparently of spontaneous origin, presents itself in a male, we must not allow the question of sex to lull our suspicions; for, although progressive pernicious anæmia is rare in males, chlorosis is rarer still. Whatever the age, sex, etc., of the patient, the diagnosis of pernicious anæmia will always derive support from our failure to obtain any adequate explanation of the symptoms, either by carefully examining the various organs, or by inquiries into the patient's history. Want of the necessaries of life, and exhausting disease, may have preceded the attack, but they are not enough to exclude progressive pernicious anæmia from our consideration. Of course, I assume that the degree of anæmia is out of proportion to the severity of the antecedent noxæ, and that the altered blood does not respond as usual to an appropriate course of tonic treatment, both causal and essential. The more fruitless all our tonic remedies, the more decided the contrast between the onward course of the anæmia and the means we employ to check it—the nutritious diet, the iron, the transfusion of blood—the more vividly will the progressive and pernicious character of this strange disease force itself on our attention while the patient is alive, and the less needful will be the evidence derived from post-mortem examination to confirm our diagnosis.

Lastly, there are a few symptoms which, though not by any means pathognomonic, afford great assistance in enabling us to recognize the disease. 1. The association of extreme pallor with a relatively insignificant degree of emaciation. This feature is common to progressive pernicious anæmia with chlorosis, and also with leukhæmia and pseudo-leukhæmia; but it distinguishes it from all other forms of severe anæmia, more especially from the cancerous cachexia, the hectic state, etc. 2. The unusual loudness and persistency of the cardiac murmurs. Just as in severe cases of chlorosis, leukhæmia and pseudo-leukhæmia, this indicates the extreme degree of the blood-change and of the consequent disturbance in the function and nutrition of the heart; accordingly, it may assist us in arriving at a diagnosis after we have eliminated the three last-named diseases. 3. The moderate dropsy that almost invariably shows itself towards the close of life. This serves more especially to distinguish progressive pernicious anæmia from chlorosis, which so closely resembles it. Dropsy is exceedingly rare in the latter affection, whereas it is common in many forms of ordinary anæmia. 4. The hemorrhagic symptoms, particularly the retinal extravasations. These are much more common in pernicious anæmia than in chlorosis or in ordinary anæmia, their relative frequency in this disease being only paralleled in leukhæmia and pseudo-leukhæmia. 5. The so-called "anæmic fever." Febrile paroxysms in the course of a severe anæmia of obscure origin must always be regarded (when the fever cannot be otherwise accounted for) with great suspicion. When we consider how constant a feature of Biermer's disease fever appears to be, especially towards its close, it seems fair to lay stress upon this symptom when we are trying to decide that a doubtful case is really one of progressive pernicious anæmia.

Although I quite admit that Biermer's anæmia may be complicated with other morbid processes of an allied kind (see p. 596), still, the latter present a sufficient number of distinctive characters to prevent all risk of error, at any rate in uncomplicated cases. I allude especially to the three diseases with which progressive pernicious anæmia seems to be most nearly allied, viz., chlorosis, leukhæmia, and pseudo-leukhæmia (*anæmia splenica et lymphatica*). If we briefly summarize the more important features of these several affections, and contrast them with those of Biermer's anæmia, we shall arrive at the following conclusions bearing on differential diagnosis.

Chlorosis is a constitutional malady which usually depends on a congenital hypoplasia of the blood; its effects generally show themselves at puberty, and almost exclusively in females. In mild cases the disproportion between the growth of the blood and that of the tissues becomes obliterated after puberty; its manifestations disappear for good without leaving any appreciable traces behind them. In severe cases, on the other hand, the disease persists, or, at any rate, shows a great disposition to recur. Chlorosis is not attended by any liability to dropsy; it is scarcely ever accompanied by fever or by any decided signs of a hemorrhagic diathesis. When moderately severe, it usually admits of being cured with surprising rapidity by suitable remedies; even when severe, it may be temporarily suppressed. Finally, when left to itself, it presents at worst a stationary, but not a progressive or malignant character. Leukhæmia and pseudo-leukhæmia, on the other hand, resemble Biermer's anæmia in running a progressive and malignant course; they also resemble it in being associated with a tendency to fever and to hemorrhage. They differ from it, however, in being attended with overgrowth of the spleen, the lymphatic glands, the marrow of the bones, etc.; and the absence of these features, or, at any rate, of the first two, may easily be ascertained by physical examination during life. Finally, leukhæmia is specially characterized by an excessive increase in the number of leucocytes in the blood, which may readily be determined by the microscope; but some caution is necessary in drawing inferences from microscopical examination, for a considerable degree of *relative* leucocytosis is occasionally met with in simple pernicious anæmia (p. 587), and may, if the state of the cytogenic organs be left out of account, lead us to confound the disease in question with leukhæmia.

On the other hand, true leukhæmia may be mistaken for progressive pernicious anæmia when, as sometimes, though rarely, happens, the hyperplasia is more active in the marrow of the bones and other inaccessible cytogenic tissues than in the readily accessible spleen and lymphatic glands. In such cases a thorough examination of the blood and of the skeleton during life, and, above all, a careful inspection of the body after death, will throw the necessary light on the case. By way of illustration, let me quote a brief abstract of the following case from the Basle Hospital. It has been published at length elsewhere.[1]

L. N., a girl of seventeen; previous health good; has been growing steadily paler and weaker for the last eight weeks. Quite lately she has begun to suffer from fever, with frequent epistaxis and a petechial eruption. On admission, corpse-like pallor, numerous petechiæ, traces of blood about the gums, fauces, and nostrils, were observed; high fever (40° C. = 104° F., and upwards); loud systolic murmurs over the præcordial region; pulsation in right jugular vein; no increase of cardiac dullness; slight enlargement of spleen. The blood exhibits a very considerable increase in the number of its leucocytes (one colorless to twenty red corpuscles). Most of the leucocytes are small, with relatively large nuclei, as in lymphatic leukhæmia. No enlarged lymphatic glands. Sternum, ribs, vertebral column, and other parts of the skeleton very sensitive to pressure and percussion.

Probable diagnosis: subacute myelogenic leukhæmia.

Death seventy hours after admission.

Sectio cadaveris.—Extreme paleness universal; petechiæ; blood shows the characters described above; extreme fatty degeneration of the heart; spleen slightly enlarged; no enlarged lymphatic glands; great overgrowth of the marrow in all the bones examined (ribs, sternum, bodies of vertebræ, femur). Numerous retinal extravasations.

In this case, which might have been taken, even on the post-mortem table, for a typical example of progressive pernicious anæmia, had the bones not been examined, a correct diagnosis during life was only rendered possible by the peculiar state of the blood and the sensitiveness of various parts of the skeleton. The characters of the blood afforded decisive proof that the primary change in this fluid consisted, not in any deficiency of red corpuscles, but in an excess of young, immature, colorless elements—in a leukhæmia. Now, as the spleen and lymphatic glands were free from the changes they usually present in leukhæmia, while the skeleton exhibited the exaggerated sensibility alluded to by Mosler as a sign of the myelogenic form of the disease, my attention was naturally drawn, even during the patient's lifetime, to the marrow of the bones, which was actually found after death to have been the principal source of the leukhæmia.

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[1] See my paper, Case III. p. 236.

Duration, Issues, Prognosis.

The duration of progressive pernicious anæmia may vary (as recorded cases show) within moderately wide limits. Inasmuch, however, as its onset is nearly always imperceptible, no precise estimate of its duration can be formed, especially in complex cases. It seldom lasts for less than six or eight weeks, or for more than the same number of months. When it comes on during pregnancy, death always takes place before the normal term of gestation is reached (Gusserow). But the chance of a favorable result is in the highest degree doubtful, even apart from pregnancy, when the disease is well marked. Our present experience justifies us in regarding every case as tending inevitably to a lethal issue. Death usually occurs under circumstances of extreme prostration; all the functions are extinguished gradually, and without any great struggle. Sometimes, though more rarely, death takes place suddenly and unexpectedly from syncope or cerebral hemorrhage. I have already stated that, when the patient is pregnant, abortion usually precedes death by a short interval. Hence, the occurrence of labor-pains in a pregnant woman suffering from progressive pernicious anæmia must be regarded as a sure sign of immediate danger, coincident with the first approach of the death-agony, and the immediate precursor of death itself.

Treatment.

So long as we are ignorant of the true causes of the disease—our etiological knowledge, imperfect as it is, relating exclusively to a few occasional and auxiliary factors—there can be no question of preventive measures or of any adequate fulfilment of the *indicatio causalis.* Experience leads me to doubt whether the removal of the auxiliary causes, where these exist, is of much use. Still, we must do all we can to combat whatever influences of the kind we may discover in any individual case; ways and means will, of course, vary with the nature of the supposed auxiliary causes. Looked at from this point of view, Gusserow's suggestion that, in progressive pernicious anæmia associated with pregnancy, premature labor should be induced as early as possible, in order to prevent inevitable death, is of great, though purely theoretical interest. I do not know if the suggestion has ever yet been carried out; even one successful case would justify us in adopting this heroic measure. In the meantime, I am not sufficiently convinced on *à priori* grounds of the benefits to be anticipated from its adoption, to venture any positive statements in its favor. I believe that pregnancy is an important predisposing or, perhaps, exciting cause of the disease; but I greatly doubt if its removal would be followed by an arrest of the disease itself.

The fulfilment of the *indicatio morbi* will naturally consist in an energetic employment of all the roborant measures at our command, viz., a nourishing and strengthening dietary, large doses of wine, iron, quinine, etc., and, above all, transfusion. Unfortunately, however, experience has taught us that not one of these measures, including transfusion (Gusserow), exerts any radical influence on this form of anæmia, or even appears capable of appreciably delaying the fatal issue. Indeed, the absolute fruitlessness of all tonic treatment and the uninterrupted progress of the disease towards death are the essential clinical characteristics of this peculiar and enigmatical affection. The name given to it by Biermer would cease to be applicable were our therapeutic efforts capable of achieving any measure of success.

We must content ourselves for the present with prescribing the above remedies, indicated as they are by reason, without any hope of doing good. The symptoms must be met as they arise. How to do this I need not explain here, for I can add nothing to the instructions that I have already given (p. 492 et seq.).

CORPULENCE.

IMMERMANN.

Corpulence.

(Synonyms: Obesity, Adipositas, Lipomatosis universalis, Polysarkia, Fettleibigkeit, Fettsucht.)

Literature.

Hippokrates, Aphorism II. 44. V. 46. Id. De salubri diaeta IV.—*Celsus*, Medecin. Lib. II. Cap. 1.—*Galenus*, Methodus medendi IX. 3.

Sebiz, De marasm. et gracilescent. sanor. et aegrotant. crassitie et obesitate natural. et morbos. Argentorat. 1658.—*Wolf*, De obesitate exsuperante. Jena, 1683. —*Schaper*, De obesitate nimia. Rostock. 1701.—*Verdries*, De pinguedin. usib. et nocumentis in corp. hum. Giess. 1702.—*Quelmalz*, De pinguedin. usib. et nocument. Giess. 1702.—*Ehrlich*, De obesorum ad mortem proclivitate. Hal. 1730.—*Walther*, De obesis et voracibus. Lips. 1734.—*Homeroch*, De pingued. ejusque sede. Lips. 1737.—*Schulz*, De obesitate. Ludg. Bat. 1752.—*Malcolm Flemming*, Ueber die Natur, Ursachen und Heilung der Fettsucht. A. d. Engl. von Plenck. Wien. 1767.—*Leidenfrost*, De morb. adip. Duisburg. 1772.—*Buchiene*, De adip. Ultraject. 1774.—*Riemer*, De obesit. caus. praecip. Hal. 1778.—*Lorry*, De la graisse dans le corpus humain. Mém. de la Société de Médec. Paris, 1779. p. 97 s.—*Ebert*, De obes. nimia et morb. in orirent. Götting. 1780.—*Jannssen*, Physiol. und path. Abhandl. von dem thierischen Fette. Hal. 1786.—*Renssing*, De pingued. sana et morbosa. Jen. 1791.—*Seifert*, Diss. phys. path. de pingued. Gryphisw. 1794.—Diction. des scienc. médical. T. XIX. p. 295. Paris, 1817.—*Craken*, De pingue et pingued. Edinb. 1805. —*Bichat*, Anat. génér. T. I. p. 54 sqq.—*Dardonville*, Sur l'obésité. Paris, 1811.—*G. J. Jaeger*, Vergl. einiger durch Fettigkeit oder colossal Bild. ausgezeichneter Kinder und einiger Zwerge. Stuttgart, 1821.—*Kuehn*, De pinguedin. imprimis hominis. Lips. 1829.—*Gruene*, De sana et morbos. pingued. Berol. 1826.—*Schlemmer*, N. östr. medic. Jahrb. I. p. 74.—*K. J. Graefe*, Graefe's und Walther's Jahrb. Vol. X. p. 367.—*Ammon*, ibidem, Vol. X, p. 427-437.—*Baumgaertner*, Bad. Annal. d. ges. Heilk. Vol. III. 2. p. 23.—*Wadd*, Comment on corpulence. Lond. 1828.—*Kreutzberg*, De polypionia. Götting. 1829.—*Fischer*, Prüfende Blicke auf das Embonpoint der Männer und Frauen. Nürnberg, 1832.—*Senofonte Taroni*, Omodei Ann. univ. di medic.

1834. April.—Recherches sur l'obésité par le Dr. K——. Paris, 1837.—*Leon de la Panouse*, Sur l'embonpoint et l'obésité. Deutsche Uebersetzung. Kassel, 1839.—*Watt*, Die Corpulenz als Krankheit, ihre Ursachen und Heilung. Aus d. Engl. nebst Zusätzen und Bereicherungen des Dr. Leon. Weimar, 1839. —*Richard*, Traité pratique des maladies des enfants. Paris, 1839.—*Ventzki*, De primelosi nimia. Diss. inaug. Berlin, 1841.—*Bowman*, Lancet, 1841–1842. V. I. p. 560 ss.—*Stark*, Allegemeine Pathologie. Vol. II. p. 281.—*Chambers*, Corpulence, or the excess of fat in the human body. Lond. 1850.—*Virchow*, Handbuch der spec. Pathologie und Therapie. Erlangen, 1854. Vol. I. p. 344. —*Wunderlich*, Handbuch der Pathologie und Therapie. Vol. II. p. 27; Vol. IV. 547.—*Roeser*, Der Fettsucht in Bezug ihres Einflusses auf den tödtlichen Verlauf bei Typhus und anderen fieberhaften Krankheiten. Memorabilien, Vol. V. 3. 1860.—*Duchesne-Duparc*, Gaz. des hôpitaux 18, 19 (1862), 8 (1863).—*Banting, W.*, Letter on Corpulence addressed to the public. London, 1864. —*E. Smith*, Lancet, I. 20, 21. May, 1864.—*Langdon H. Down*, Lond. Hosp. Rep. I. p. 97 (1864).—*Menville*, Gazette des hôpitaux, 1864. 44.—*Daniel*, Bulletin de thérap. LXVII. 1. p. 44. 1864. Id., Physiologie appliquée, etc. (1865). Paris. Delahaye.—*Virchow*, Archiv. Vol. VIII. (1855) p. 537. IX. p. 281; Die krankhaften Geschwülste I. p. 364; Cellularpathologie IV. (1870) p. 400–432. —*Czajewicz*, Archiv f. Anatomie, Physiologie, etc. (1866), p 289.—*Kuehne*, Lehrbuch der physiol. Chemie. Berlin, 1868. p. 365–382.—*J. Vogel*, Corpulenz, ihre Ursachen. Verhütung und Heilung u. s. w.—*H. Meissner*, Schmidt's Jahrbücher Vol. CXXVII. (1865) p. 168.—*Schindler*, Reductionscur zur Verhütung und Heilung der Fettsucht. Wein, 1868.—*Voit*, Zeitschrift f. Biologie. Vol. V. p. 79–169 (1869); Vol. V. p. 329.—*Ssubotin*, ibidem, Vol. VI. 1, p. 73–94 (1870).—*Flemming*, Centralbl. d. med. Wissenschaften, VI. p. 481–3 (1870); Archiv f. mikroskopische Anatomie, VII. p. 32–80 (1870).—*Toldt*, Sitzgsber. der k. k. Academie zu Wein. Math. naturw. Cl. Vol. LXII. 2. p. 445–467.—*Radziejewski*, Virchow's Archiv, Vol. XLIII. p. 268 ff.—*J. Bauer*, Zeitschrift f. Biologie, Vol. VIII. (1872) p. 567.—*F. Hofmann*, Der Uebergang des Nahrungsfettes in die Zellen des Thierkörpers. München, 1872 (Habilitationsschrift).

Historical Sketch.

That distinction which we make between "fat" and "thin," as regards the external appearance of individuals, and through which so essential a part of our inner somatic *lot* (Geschehen) (to use the word in its most precise sense) typically expresses itself, has undoubtedly existed everywhere and in all ages; and among these "fat people" there have, always and everywhere, been some "uncommonly fat people," whose immoderate circumference and abnormal corpulence have obtained for them a popular celebrity. To attempt to trace the history of this adipose disease from its origin in antiquity would be a hopeless task, for the affection being undeniably as old as the human race itself, or, at any rate, as civilization, with civilization it is indeed genetically related, inasmuch as its development is clearly influenced by many conditions resulting therefrom.

To this very circumstance the affection owes its popularity, and the corpulent patient himself the rôle he has from time immemorial played in the motley fair of life, among all cultured nations; for the knowledge that certain human weaknesses which, however amiable they may be, still remain weaknesses, often plainly conduce to the production, the pathological conditions, of corpulence soon forces itself upon the consciousness of the masses, and taken in connection with the peculiarity of the corpulent *habitus*—the disproportion between height and girth, the ludicrous clumsiness of movement, etc.—stamped the corpulent man once for all as a comic figure, strive as he might against such an estimate. As an involuntary comic character he was therefore always a welcome and remunerative subject for art, as soon as it began to descend from its ideal height, and, abandoning the sublime, to permit the burlesque genus in its turn to find expression. And if it be the most difficult problem for true art, in representing a mean object, while preserving the truth of nature in the portrait, to shed over it the illuminating gleam of the ideal and of poesy, who will not frankly acknowledge that the corpulent man has obtained the honor and glory of the fullest artistic portrayal! For who that gazes with admiration upon the antique plastic representations of the Bacchic rout can behold the old fat-bellied pedagogue Silenus, surrounded, upheld, and borne along in the train of the ever-young and folk-compelling god, by the wanton race of long-eared fauns and goat-footed satyrs; who can delight his soul with the prudent life-lore and quaint rogueries with which Sir John Falstaff, a second Silenus, amid his followers daily and nightly enlivens the frolics of the young Prince Henry, a second folk-compeller, without feeling himself—temperate son of this weighing and measuring nineteenth century though he be—still deeply stirred by those primordial pleasures that once moved the men of Greece and the contemporaries of Shakspeare? Let us hope that even our great-grandchildren may be made partakers in them through frank companionship with these masterpieces of plastic and dramatic art. A reference to these two figures, both alike noble and classic, is sufficient aptly to indicate the prominent place that "the fair, round belly" has lastingly won for itself, as a comic type, in the popular mind as well as in the realm of popular art.

It is, however, more to the purpose at present, briefly to notice those more practical efforts which have had for their object the prevention or removal of this disease, and which have originated partly in the insight which has been acquired as to its genesis, and partly also in a recognition of its evil consequences. The classic nations of antiquity in particular engaged in such practical efforts with a zeal which might fairly astound us did we not know what a fine natural power of observation was possessed by those most prominent representatives of ancient culture, the Greeks, and how strenuous were their endeavors practically to realize their ideal then and there in the world of every-day life. The gymnastic exercises so passionately practised by the Greeks, and in which so essential a part of their national education culminated, had then for their express object, according to the unanimous testimony of their historical and philosophical writers (Thucydides, Plato, and Xenophon), the prevention of great corpulence. A huge padding of fat not only shocked the highly developed æsthetic sensibility of this richly gifted people, but was most justly regarded by them as a hinderance to corporal robustness. But in order to make the young man not merely beautiful, but in an especial degree strong and capable of endurance, and thus fitly to fashion him for his country's ends, he was, in Greece, from childhood exercised daily with indefatigable perseverance in running, wrestling, boxing, discus-throwing, etc., so that the prophylaxis against corpulence was formally elevated into a state principle, and as such occasionally carried out with reckless energy. How far this recklessness went in some Grecian States, and how much in concert they were as regards the prevention of corpulence, the Spartan method of education shows with the utmost clearness. For, according to the intention of their great lawgiver, Lycurgus, among other important things it was calculated to prevent the occurrence of corpulence in Lacedæmon, as its deteriorating influence upon the bodies and minds of the young citizens appeared to this father of the Spartan constitution to be highly detrimental to the commonwealth. Take Plutarch as an authority, where, in the *Life of Lycurgus* (chap. 17), he describes the education of the Spartan youth:

> "Their meals were always very frugal, so that they were compelled to think of the appeasing of their stomachs, and thereby to become bold and crafty. This was one object of their meagre diet, *the other must have been the development of their bodies.* For if the vital spirits be not burthened with an excess of nourishment and pressed into the depth and breadth, but are permitted to sustain their ethereal essence, the body can increase free and unhindered, and *thus becomes slender in its growth.* A thin, slender body is better suited for strength and a fine conformation than a thicker and better nourished one, which by reason of its heaviness resists," etc.

This being the case, it is not strange that physicians also have given their attention to a morbid condition with which even the state attempted to grapple for the sake of its own interests as well as those of the individual. We find, then, as early as the writings of Hippocrates, not only a very remarkable knowledge of certain evil results of corpulence (such as the lesser tolerance of acute diseases by fat individuals,[1] the frequent coincidence between corpulence and sterility in the female sex,[2] etc.), but also prescriptions, as strict as they are concise, regarding the regimen to be maintained by "such as are desirous of becoming thin" (*ὅσοι βούλονται λεπτοὶ γίγνεσθαι*).[3] A hard bed; hard bodily work early in the morning, on a fasting stomach; a vegetable diet, especially green vegetables, after this early work is done; the diligent practice of running round in a circle every day in the open air in the costume of Adam—these are the outlines of this antique method of cure, beside which our modern Banting system certainly appears mild, and which does not gain in pleasantness from the further directions—to abstain from the warm bath, and to take wine only when diluted with a great deal of water.

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[1] Aph. II. 44.

[2] Aph. V. 46. Hyppocrates supposes the cause of such sterility to be the pressure of the fatty omentum upon the mouth of the womb, and its mechanical occlusion in this manner.

[3] *De salubri diæta* (περὶ διαίτης ὑγιείνης), Cap. IV.

Among the later physicians of antiquity, Celsus and Galen occupied themselves with corpulence; and both, like Hippocrates, call attention to the dangers which threaten the corpulent: sudden death, the tendency to succumb under diseases attended by fever, and the "putrid," that is to say, *asthenic* character of the fever in such cases. It is known, moreover, that Galen traced the disposition to corpulence to an excess of one of the four cardinal humors assumed by him, namely, *phlegma*, and that accordingly with him originated the doctrine of the frequent coincidence of the phlegmatic temperament with the corpulent diathesis.

We may, without being inexact, boldly skip over the whole range of the following centuries, medieval and modern, simply resuming the thread of our historic remarks where, in the present century, modern physiology begins to occupy itself more particularly with the question of the origin of animal fat.

No medical author, either of later antiquity or more recent historic times, has in his observation upon corpulence, so far as the affection is casually mentioned in those writings which touch upon it, added anything to the doctrine of Galen; and the more important works of the seventeenth and eighteenth centuries referred to in the literature of the subject, stand one and all on the same ground—for the most part dealing only with particular cases of abnormal corpulence, or with discussions concerning the evil consequences and dangers of the affection, especially as manifested during the progress of intercurrent diseases. This latter point is always with perfect correctness seized upon in the clinical observation of the disease and insisted upon in the description; but in the ordinary relations of life the affection produces an evil result, which exposes the patient to very considerable inconvenience, and all sorts of social vexation, but which is in general pretty well borne so long as no extraordinary demand is made upon the functional and resisting power of the organism by some other grave disease. Roeser has likewise in modern times (1860) proclaimed the slight tolerance of febrile diseases, such as typhus, by corpulent patients, thus giving expression to a thought which we find expressed in almost the same form by the great physicians of classical antiquity.

On the other hand, the disease has comparatively seldom been made the subject of a special monograph even in recent times. We may here particularly mention the treatises of Lischer (1832), Watt (1838), Léon de la Panouse (1839), which we meet as references in the literature of the subject, and last but not least, the excellent work of J. Vogel (1865), the publication of which was occasioned by W. Banting's letter to the public (1864), which, whimsical as it was, was full of practical value and made an epoch in the treatment of the disease.

This letter itself, however—or rather the therapeutic system which it communicated to the public, that of Dr. Harvey, to whom Banting had applied when in need of advice—had its root in those new investigations respecting the production of fat in the bodies of animals, to which J. von Liebig gave the first impulse. With whatever justice subsequent investigators have called in question some of Liebig's views respecting animal lipogenesis (the development of animal fats from the hydrocarbons, for instance), his name remains connected with this, as with much else that marks him as the opener up of new paths, that with him originated a clearer understanding of the fundamental laws of physiological chemistry (*Stoffbewegung*), and a deeper insight into the nature of fat-production as a general function of the organism. Among those authors and investigators whose labors in physiological chemistry have most advanced our knowledge of the conditions of normal and abnormal fat formation during the last two decades, we may especially mention F. Hoppe-Seyler, M. von Pettenkofer, C. Voit, Kemmerich, Ssubotin, Radziejewski, and Fr. Hofmann. Their investigations revealed for us the sources in which animal fat has its origin, the mode of its production, the conditions which favor or retard its development, and its particular significance as regards the general well-being of the organism ; so that at the present day, as we stand upon the vantage-ground won by their labors, the question concerning the pathology of corpulence may be answered, at least from the standpoint of chemical physiology, much more precisely than before. Much less can be said for the histological side of the question. Here the opinions of authors stand in much ruder opposition; and the position of the so-called fatty tissue (Fettgewebe) in the histological system, the mode in which it plays its part in the predisposition to fat formation; in short, the nature of the local conditions which exist during fat production, is as yet by no means satisfactorily ascertained. We may name Virchow, Czajewicz, Toldt, and Flemming, as among the number of those who have occupied themselves more particularly with the histological study of the *tela adiposa* and its behavior in the healthy and in the corpulent, and have imparted their discoveries in exhaustive works. We may now hope that future explorations will fully clear up this territory, and that with the settlement of these still pending differences of opinion (see the following section on Pathogeny for a more detailed account), a further and more important step may be taken toward the understanding of both normal and abnormal fat production. No one who occupies himself with this chapter of pathology can escape the conclusion that the pathology of corpulence, from its very nature, can only be comprehended by the help of chemical and histological investigations.

General Description of the Disease.

We are accustomed to designate under the term *corpulence* (adipose disease, adiposity,[1] polysarkia, etc.) all those anomalous conditions of physical configuration which have as their prominent outward mark an excessive development of the subcutaneous layer of fat, as well as a corresponding unshapeliness of the figure. An examination of the dead body proves, however, that the abnormal heaping up of fat in corpulent persons is not confined to the *panniculus adiposus*, or the external fat of the body, but takes place with great regularity in certain deeper regions as well. In fact, where we normally find, in well-nourished, healthy persons, fat in still larger masses—the so-called *visceral* fat—(viz. : in the mesentery, the *omentum*, *capsula adiposa* of the kidney, *epicardium*, etc.), we find it, on post-mortem examination of the corpulent, in layers of abnormal thickness. It is accordingly quite characteristic of the affection with which we have to deal, that the morbid tendency to over-growth attacks *not merely certain limited portions of the tela adiposa, but the fatty tissue all over the body. The great multiplicity of morbid centres and their universal extension throughout a certain tissue formation* (*histological homology of the seat of the disease, or homoiotropy*) in all probability mark the anatomical changes presented in corpulence as the expression of a *general morbid condition*, or as the *localization* of a *constitutional* affection. But as these changes, taken collectively, most distinctly bear the stamp of *homoiotropy* (or *histological homology*), that is to say, everywhere unmistakably prove themselves products of definite pathological processes, and also everywhere evidently take place in the same manner, they at all events unite in themselves with the greatest possible completeness all those signs which usually characterize the local emanations of constitutional affections. No doubt can therefore remain, regard being had to these most universal anatomical criteria of corpulence, that in this affection we have to deal with a *general lesion of the function of nutrition.*

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[1] Instead of this term the shorter word adiposis is frequently used. We avoid using it ourselves because it is certainly a false etymological compound, being a Latin derivative with a Greek termination.

This histological change in the fatty tissue of corpulent individuals essentially involves a twofold pathological process. First of all there takes place in the entire mass of the fatty tissue, already extant, and formed before the invasion of the disease, a steadily advancing infiltration and distention of the cell-elements with fatty contents; and subsequently there occurs an enormous development of new fatty tissue, which, like the old, develops in the affected regions of the body, especially predisposed to fat production, in the form of little lappets, the so-called fat-clusters (*Fetttr\u00e4ubchen*). Both processes—the distention of the cells of the already existing fatty tissue, and the development of new—concur to produce that increase in volume of the fat-carrying layers of the body which is often so enormous; and, since their influence upon the volume of the *tela adiposa* goes on simultaneously, it is practically extremely difficult to distinguish perfectly between their periods of origin; for, even though it may appear as if the infiltration of the pre-existing fatty tissue represented a somewhat earlier, and the springing-up of new tissue a later stage in the general progress of the complex pathological process, the cell-distention still continues in all cases in the existing fatty tissue, even when new tissue of this kind is in process of formation; and further, though the latter process takes the foremost place in the severer, and the former in the rudimentary forms of the disease, both are in all cases so intimately connected, in locality as in time, and intertwine themselves so inseparably, that it is from the first simply impossible, from this standpoint, to distinguish between any two stages of corpulence. It is, however, clear, from this very coincidence of two essentially different lesions, that some inner genetic connection must exist between the two. This presumption becomes almost unavoidable when we consider that, even within the limits of health, both processes continually go hand in hand, in locality as in time, in this wise: that, in the *first* place, individuals who, without being morbidly fat, are of a rather full habit of body, possess not only a more strongly infiltrated fatty tissue (better filled fat cells), but also *more* fatty tissue, than thin persons; and *secondly*, that in thin persons who, in consequence of certain known influences (richer food, for instance), begin to appear "in good condition," not merely the mass, but the quantity of the fatty tissue is increased. Since, therefore, even under physiological conditions, that proportion between mass and tension of the fat cells can be proved to exist with the utmost regularity, there is surely all the less opportunity offered for regarding as an accidental coincidence that excess in both directions which comes under anatomical observation in the condition of pathological corpulence. It is, moreover, evident that, so soon as it is in any way possible to discover a sufficient reason for this physiological coincidence, an explanation of the simultaneousness of the two processes under pathological conditions may also be immediately found. (See section on Pathogeny.)

In one respect, however, there appears at first sight to be an essential difference, and not merely one of degree, between simple physiological "good condition" and morbid corpulence inasmuch as, at least in advanced cases, deposits of fat frequently occur in tissues in which in the healthy subject no fat is discoverable on microscopic examination.

We find, under some circumstances (see farther on), the intramuscular connective tissue, and even the epithelium of the urinary tubules, etc., infiltrated with fat, and this is especially the case with the liver-cells, which, in the better-marked cases of adiposity, ordinarily become the seat of a continual fatty impaction, while, under physiological conditions, as we know, they are but transiently percolated by a stream of fat—always merely at certain hours, after a fatty diet (Virchow[1]). We shall subsequently find an opportunity of going into this point again, and of showing that this heterology between a pathological and physiological tendency to fat production is at bottom merely an apparent one, and that really it is hardly necessary to recognize in morbid corpulence anything more than the excess of a process which, taken *per se*, is a normal one (cf. "Pathogeny" and "Special Symptomatology").

If we disregard the above-mentioned rather exceptional conditions of many tissues in the more pronounced types of corpulence, and observe once more the histological character of the rudimentary forms of the disease, we find them, as we have remarked, even superficially, so completely homogeneous with the physiological characters of so-called "embonpoint," that it is impossible to draw sharp boundary lines between the two. Let us further consider that each of these advanced cases had itself previously to pass through an "embryonic" stage, in which it was scarcely, if at all, distinguishable from healthy "embonpoint." The unbroken connection between a physiological and pathological tendency to fat-production then becomes quite obvious. We must, then, frequently remain in doubt as to whether one of these cases of slightly developed corpulence, or more pronounced "good condition," should be regarded as *already morbid* or *still healthy*, and the question as to its morbid character can certainly not be incontrovertibly answered either in the affirmative or negative. From this ambiguity of many cases of rudimentary polysarkia, two consequences follow when we come to decide upon the nature of the disease with which we are concerned. In the *first* place, it is just as little possible in dealing with corpulence, as in dealing with anæmia, to express a decided opinion as to its frequency, that is, to draw up a *statistic* of the disease; and secondly, the *pathogeny* of the disease points to precisely the same conditions and factors that determine the amount of *physiological* tendency to produce fat. In what these more particularly consist will be treated of in the following pages, so far as the discussion of this subject is necessary, as briefly as possible; but we may here remark, in general terms, that corpulence, as a disease, from the *physiological* as well as from the purely *histological* standpoint, is to be classed as a *constitutional* affection, or *lesion* of *general nutrition.* It is known that fat-production in the bodies of animals is eminently at the expense of a function of the whole organism, individual and temporary fluctuations of which are determined by existing conditions of the general nutritive process—the amount of the pabulum, rapidity and mode of its assimilation. This helps to strengthen the presumption that, as regards the etiology of corpulence (*vide* "Etiology"), the causes of the disease make the entire constitution, or the interchanges between the blood and the tissues, rather than any particular organic apparatus, their point of attack. We shall endeavor to bring this forward in detail in a more suitable place, so far as it is at present possible to give a direct proof of such a relation between particular predisposing forces and determining noxious agents. We must, however, cut short these preliminary observations, in order first to investigate the *pathogeny* of the disease in the direction already specified.

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[1] In his Archiv. Bd. XI. p. 574.

Pathogeny.

It is known from physiology that the store of fat at any time laid up in the animal body is derived from the nutriment assimilated by the organism; so that the magnitude of this store is primarily determined by the amount of the *ingesta.* An increase of the fat-store, or a so-called fatty "habit" takes place, therefore, in one and the same individual only when, other conditions being the same, the amount of nutriment is increased; and a decided tendency to this fatty habit can only be produced by a still greater assimilation of food. This is taught by every-day observation, which coincides with exact experiments in fattening animals. On the other hand, there is no surer method of producing diminution and final disappearance of the fat of the body, internal and external, which is stored up in the cells of the *tela adiposa*, than diminution or withholding of nourishment (partial or complete inanition). A determination of the comparative weights of the various organs and tissues of the body in such cases, gives, as we know, the important result that, of all tissues, the fatty tissue suffers the most remarkable diminution in weight, owing to the absorption of its fatty contents. (See "Anæmia," p. 372.) Hence it follows that no component part of the living organism varies so remarkably with the amount of food as the fat-store, or fat which is laid up in the fatty tissue, or is more dependent upon the assimilation of nutriment.

With regard to the further question, *from what elements of the food animal fat is principally derived*, the more recent physiological view, which differs, as we are aware, from that formerly held, regards the greater portion of the fat-store as probably a product of the decomposition of the *albumen of the pabulum* (Vorrathseiweiss), just as the fat which occurs in degenerative processes is a product of the decomposition of the *organized albumen* (Organeiweiss).

More minutely observed, especially in the development of fat from the albumen of the pabulum, the following process takes place: The albumenized materials taken in with the food and circulating with the fluids of the body, so far as they are not directly employed in the repair and growth of the albuminous tissue-elements, become transformed into organized albumen (Voit); and in consequence of the chemical changes that take place in the cells there is a decomposition, *first*, into nitrogenized derivatives, which, further decomposed and oxidized, are at length, by means of the great diffusibility of the finally resulting products (*urea*, *uric acid*, *etc.*), eliminated through the excretory organs (*kidneys and skin*); *secondly*, into non-nitrogenized substances, which, in certain circumstances (*see farther on*), similarly undergo further oxidation and decomposition, and may be finally resolved into the simple chemical products, carbonic acid and water. Under other circumstances, however, and more frequently, they furnish the principal material for the production of fat, and make possible a corpulent habit. It is clear, therefore, first of all, that one condition of the free development of fat is a considerable accession of fat-producing material, and particularly albumen, to the pabulum in circulation, and further that the degree of disposition to fat-production is regulated very essentially by the *ultimate fate of the albumen of the pabulum.* It may be especially laid down that, the accession of albumen remaining the same, *first, the smaller the quantity of organic albumen formed, and, therefore, the greater the quantity of the circulating albumen which undergoes but partial decomposition ; and secondly, the more unfavorable the circumstances for a further burning away of the non-azotized products of decomposition to carbonic acid and water, the greater will be the quantity of fat produced from the albuminates.*

The opinion that fat may originate in the decomposition of albumen, necessitated as it is by a vast number of facts, physiological as well as chemical and toxological, is at the present time seriously attacked by no one. It is, indeed, impossible for us here to argue out this subject *in extenso.* We, however, adduce the principal methods of proof upon which the theory has hitherto rested, making free use of Wagner's synoptic arrangement,[1] and completing it. These methods of proof are, as we have already intimated,

a. *Physiological, such as :*

1. The results of Pettenkofer and Voit[2] in feeding a carnivora (*dog*) with a great quantity of lean meat. The animal experimented upon excreted all the nitrogen contained in the food in the form of urea, but, as experiments on the respiration proved, retained a portion of the carbon. This portion of carbon must, therefore, have been stored up in the form of an anazotized product of the decomposition of muscular albumen.

2. The character of the milk of a carnivora (*dog*) on a pure flesh diet. Under these circumstances the quantity of this secretion, as also its richness in fat, increases with an increasing supply of albumen (Ssubotin,[3] Kemmerich[4]).

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[1] A Manual of General Pathology, by *Ernst Wagner*. Transl. from the German by J. Van Duyn, M.D., and E. C. Seguin, M.D., p. 300 et seq. New York, 1876.

[2] Zeitschrift f. Biologie. Bd. V. p. 79–169.

[3] Virchow's Archiv. Bd. XXXVI. p. 561–572.

[4] Archiv f. Physiologie. Bd. II. 7, 8. 401–415.

3. The character of the milk of an herbivore on a diet of ordinary richness. In this case the fatty contents of the milk exceed those of the food, while the albuminous contents of the food are always sufficient to cover the production of the milk-fat (Voit, l. c., Kuehn, Fleischer[1])

4. The considerable increase in the production of wax (melissyl palmitate) by bees fed on the albumen of hen's eggs and sugar-candy, in proportion as the albumen in the food is increased (Fischer of Vaduz).

5. The increase of fat to two or three times its former amount contemporaneously with a decrease of albumen, observed by Burdach during the development of the eggs of a species of mollusk (limnæus stagnalis).

6. The perceptible tendency to fat-production in the bodies of the larvæ of flies while fed with defibrinized blood poor in fat (Fr. Hofmann, l. c.).

b. *Chemical.*

1. The formation of the so-called "corpse-tallow" (Adipocire), which replaces the normal tissue in muscles slowly putrefying in cold flowing water.

2. The diminution of casein, with a simultaneous increase of fat, in Roquefort cheese which has lain by a long time (Blondeau).

3. The increase of fat in milk on exposure to the air (Hoppe-Seyler,[2] Ssubotin, l. c.).

4. The development of leucin (amido-capronic acid) in the putrefaction of albumen and in digestion.

5. The formation of the lower members of the pionic acid group (formic, propionic, butyric, valerianic, and capronic acids) in the putrefaction of albuminous substances, as in their destruction with caustic potash.

c. *Toxological.*

To this head we must, above all, refer the enormous development of fat in almost all the organs (especially the muscular tissue of the heart, the liver-cells, and renal epithelium) in acute phosphorus poisoning (Koehle, Ring, Lewin, Munk and Leyden, Wagner, and many others), with a simultaneous and very remarkable increase of urea, as being the azotized final product of the albuminates (Storch,[3] J. Bauer[4]).

Even though the acute fatty degeneration which occurs in phosphorus poisoning be not histologically comparable with the simple fatty infiltration of the tissue in corpulence, it is still a most weighty argument for the chemical fact that fat is specially prone to develop from albumen, and that frequently, when it exists in the bodies of animals, it must be regarded as a product of the decomposition of albumen.

Where, however, *the quantity and composition of the ingesta remain the same*, the greater or lesser development of *organized* albumen from the circulating albumen of the pabulum, must depend upon the different disposition of the tissue in each case, as regards its mode of deriving nutriment from the blood, and of utilizing this in its growth (see p. 306). We may therefore say that, under similar nutritive conditions, *the less* the trophic and plastic energy of the tissue-elements, the greater will be the tendency to fat-production; and that all conditions (individual and general, outward and inward) which diminish the former must favor the occurrence of corpulence (see "Etiology.")

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[1] Virchow's Archiv. Bd. LI. p. 30–41.

[2] Virchow's Archiv. Bd. XVII. p. 417.

[3] Den acute Phosphorvergiftning. Copenhagen, 1867.

[4] Zeitschrift für Biologie. Bd. VII. p. 63.

The question whether *the non-nitrogenized products of the decomposition of the albumen* of the pabulum shall finally *settle down in the form of fat*, or, *more completely burnt off*, *be changed into carbonic acid and water*, is, under ordinary circumstances, primarily decided by the quantity *of the other components of the diet*, taken in simultaneously with the albumen—especially the *fats*, *hydrocarbons*, *and glutens*. The importance of these in the process of nutrition has been already illustrated and insisted on by us (see p. 312); we shall, therefore, merely remind the reader that the substances named, by their tendency to oxidize and decompose more easily than the circulating albumen, generally favor the deposition of the organized albumen as much as they retard the further oxidation of the non-nitrogenized products of the decomposition of the albumen of the pabulum. Since they require for their assimilation a great part of the available oxygen of the blood, they necessarily contribute, at least indirectly, in a very essential manner, to the formation of fat. (As regards fat see farther on.) In consequence of this, besides an increase in the organized albumen, we must expect a richer production of fat from the albumen of the organism, *in proportion to the quantity of those other substances already mentioned, which, in addition to a sufficiency of albuminates, are taken in with the food, assimilated, and added to the mass of the blood as available plastic material.* But, *in the second place, the quantity of the blood-oxygen at all times generally available* naturally calls for special consideration, as it bears upon the process which now interests us, viz., the development of fat from albumen. Suppose that, from any cause, but a small quantity of oxygen, as compared with the amount of food, be taken up. It is manifest that this circumstance is unfavorable to the more complete consumption both of the surplus matter circulating in the blood, and of the non-nitrogenized products of the decomposition of the albumen of the pabulum, and that, under these conditions, a portion of the ingesta is more than ordinarily likely to remain imperfectly consumed. *All circumstances, therefore, which occasion a diminished absorption of oxygen, also favor the formation of fat from albumen,* and must, as may be foreseen, where they actively manifest themselves to any considerable extent, lay the foundation for the development of *morbid corpulence.* (See "Etiology.")

On the other hand, *even a rich diet by no means* necessitates any considerable deposition of fat, which indeed can never take place either while the trophic and plastic processes go forward with uncommon activity (see above), or sufficient oxygen is absorbed to effect a complete consumption of the *ingesta* (the other constituents of the food as well as the albumen). *All circumstances, then, that increase the trophic and plastic energies of the tissues, or favor the absorption of a great quantity of oxygen,* work against the tendency to corpulence, and guarantee, even in cases of high feeding, *a certain immunity from morbid fat-production.*

We have, so far, for the sake of simplicity, and without much compromise of truth, merely spoken of the development of fat from albumen. We must now ask whether the *remaining* elements of the diet, whose indirect bearing upon the tendency to corpulence we have already noted, may *directly* play their part in the formation of fat.

This question must, in the present state of our knowledge, be most decidedly answered in the affirmative, as far as *the fatty portion of the diet* is concerned (F. Hofmann); while a certain proof of the development of fat from the hydro-carbons is as yet *not* forthcoming. On the contrary, the results of experiment almost certainly exclude this mode of animal lipogenesis (Voit). It is therefore not permissible to transfer the conditions which affect vegetables (in which a considerable development of fat from *starch, mannite,* etc., takes place) to the animal organism, and we should particularly remember that the plant brings forces to bear upon the isolation of atoms and the reduction of compounds rich in oxygen to a much greater extent than the animal can. We have just as little proof that fat can arise, in the animal body, from the gluten of the diet (Bischoff and Voit); yet these substances, like the hydro-carbons and fats, possess, though in a less degree, the property of protecting the already existing fat from further destruction. The lipogenous influence of these two species of food-elements (the hydro-carbons and glutens) is, then, apparently reducible to what we have already briefly stated it to be—a conservative action. Such an action they have upon the organized albumen as well as that of the pabulum, and may, consequently, of course (though but indirectly) play a very important part in the amassing of fat in the bodies of animals.

It is otherwise, as already indicated, with the fats of the diet, whose property of direct lipogenesis was formerly accepted without further investigation, while more recently, since the development of fat from albumen has been positively ascertained, it became for a short time a matter of grave doubt (Toldt, Ssubotin). This mode of fat formation—that of its simple accumulation from the non-nitrogenized material introduced into the body with the fats of the food—has been placed beyond all doubt by the painstaking investigations of F. Hofmann. It is now, indeed, even recognized as a normal process more or less regular in its occurrence. According to the above-named author, definite portions of the fat of the diet remain over, their amount depending on that of the daily receipt and consumption of the body (always determined by rest and labor); and these, like the fat separated from the albumen of the pabulum, are taken up into the general store of fat.

This is only true, however, in the case of those fats which are *homologous*—that is, which occur as *normal constituents* of the fat-store of the zoological species with which we have to do. Heterologous fats[1] are either not taken up into the fat-store of the body at all, or only taken up in the merest traces. (Radziejewski, Ssubotin.) The influence of the heterologous fats sometimes introduced with the food is, then, like that of the hydrocarbons and glutens, apparently confined to the above-mentioned conservative action—that is to say, it becomes oxidized in the place of the organized albumen, of the fat secreted from the albumen of the pabulum, and finally of the homologous fat taken in with the food, and thus protects both the latter from destruction.

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[1] Thus, not a trace of spermaceti (monatomic cetyl palmitate) found its way into the subcutaneous connective tissue of a dog, even after thirty-one days' feeding, and after more than 1,000 grammes of this heterologous fat had been consumed (Ssubotin, l. c.). Just as little has Radziejewski (l. c.) succeeded in certainly ascertaining the pres-

We must abstain from entering upon a demonstration of the foregoing points *in extenso*, as this would involve the citation of a mass of evidence obtained by experiments which would far exceed the limits allowed for our exposition. Those of our readers who wish to obtain more precise information respecting these very complicated questions will find the original works of the authors named in our notes, and the hand-books of physiology, their best guides.

Meanwhile, so great is the importance to the pathologist of this fact of the direct development of fat from the homologous fats of the diet, that we cannot refrain from briefly explaining the method of experiment pursued by Fr. Hofmann, and the principles of his calculation. An animal (*dog*) in which the fat-store is completely exhausted by long continued fasting, from this given moment of time begins to destroy its organized albumen in great quantity, to supply means for its most necessary expenditure of force; and in consequence of this change of the mode of disposition of the tissue materials, the formation of urea, up to this time greatly diminished, will suddenly increase. Suppose now that such an animal, become almost fatless from starvation, be fed for some days on a diet as rich as possible in fat, then killed, and its general condition as regards fat estimated,—if the quantity of fat in the whole animal be very much greater than that which (taking the highest calculation) could arise from the decomposition of the albuminates of the diet, it affords proof of a direct lipogenesis from the fat introduced in this diet. Now experiment evidently spoke in favor of a direct transference of the fat of the diet to the body of the animal experimented on, as the following short data show:

During the five days of the experiment, the quantity of fat taken in with the diet and assimilated, amounted to 1854.0 grammes.

The quantity of nitrogen taken in with the food amounted to 39.7 grammes.

This latter quantity corresponds to 254.3 grammes of dry albumen. Now, according to Henneberg, from the decomposition of 100 grammes of dry albumen (equal to 15.61 per cent. of nitrogen), 51.4 grammes of fat are developed, which

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ence of erucin (triatomic ether of glyceryl with erucic acid) in the body of the animal experimented on (a dog), after feeding with a great quantity of rape-oil. The ordinary mammalial fats (human fat included) are, as we know, a compound of triatomic ether of glyceryl with palmitic, stearic, and oleic acids.

would therefore give 130.7 grammes as the maximum quantity of fat which could be developed in the progress of the experiment, if all the fat accumulated during this time had simply originated in the albuminates of the diet. But the estimate of the whole quantity of fat in the whole animal showed a total of 1352.7 grammes. There was therefore accumulated during the five days of the experiment a quantity of fat greatly in excess of this estimate (by more than 1000.0 grammes in fact); and this could only have originated in the fat of the diet. All that concerns the special methods pursued by Hofmann in estimating the total quantity of fat in the animal may be read in his original work.

In a more complete form the at present received physiological theory of animal lipogenesis, which is calculated to throw light upon the pathogeny of corpulence, is briefly as follows:

> "The fat-store of the animal body is renovated and increased from the *albuminates* and *homologous fats* of the food supplied, the *remaining constituents* of which (heterologous fats, hydrocarbons, glutens) have mainly a *conservative* action upon the fat *already formed*, but are *not directly lipogenetic.* The conditions for the *accumulation of fat* are most *favorable* when the quantity of the *fat-forming* and *conservative* (indirectly fat-forming) elements of the diet is *greatest;* when *the quantity of oxygen in the blood is least;* and when *the trophic and plastic energy of the tissues that absorb albumen is smallest.*"

The pathogeny of corpulence must, however, besides dealing with the question of the sources of animal fat, and the general conditions which favor its accumulation, inquire into the more local relations between certain forms of tissue-production and fat-production. It is necessary, in short, to know not merely *whence* fat originates, and *when* the greatest quantity will be developed, but also *in what manner* it is accumulated, and how this accumulation goes forward locally.

The opinions concerning these last points, as we have already mentioned in the historic introduction, differ so much from one another in many important respects that, pending further more decisive investigations, we must restrict ourselves to a cursory statement of them; and, while noticing their most salient points of difference, will especially dwell upon what they have in common.

One idea (Toldt, l. c.) is that the deposition of fat occurs in all places where there exists normally and already formed a certain *peculiar* kind of tissue—*fatty-tissue* (*tela adiposa*). There are, in fact, parts of the body in which, through the absence of this tissue, even under conditions favorable to fat formation, no deposition of fat worth mentioning occurs (scrotum, penis, clitoris, nymphæ, eyelids, skin of the nose, muscle of the ear, sub-muscular connective tissue of the intestines, etc.). In other parts, external and internal, there are, on the contrary, great depots of this tissue, and hence, under circumstances favorable to fat-production, a vast accumulation of fat takes place (the malar region of the face, panniculus of the breasts, anterior wall of the abdomen, mediastinum, epicardium, great omentum, *capsula adiposa* of the kidney, buttocks, etc.). This fatty tissue should not be classed with connective tissue as regards either its histological relations or its functions. It has its origin, as comparative embryology teaches, not in ordinary connective tissue, but in special embryonic territories; and it is, moreover, connected with already existing fatty tissue. The cells specially adapted for taking up fat—the *fat-cells*—are polygonal or round, are without the processes of ordinary connective tissue cells (Kuehne), and appear in this individual form when they have little or no fat in them, as, for example, in the subcutaneous fatty tissue of the fœtus, or in such adults as have been quickly deprived of their fat-store in consequence of marasmus. It is further characteristic of the fatty tissue that it possesses a peculiar system of blood-vessels, the fat cells being woven round with a thick capillary plexus, which runs in a tender framework of ordinary connective tissue. There is, moreover, an agglomeration of the fat cells into small gland-shaped bodies, the so-called "fat clusters" (Fettträubchen). This mode of arrangement fails only in the fat-containing marrow of the bones, where some of the fat cells lie between the other elements of the marrow.

According to this conception of the fatty tissue, as a special *histological* element of the body, its *physiological function* is also one peculiar to itself, and consists in its separation of fat from the blood. It is true that the cells of other tissues (the liver cells, for instance) sometimes temporarily and sometimes under pathological conditions, permanently become infiltrated with fat, at such times, in fact, as the blood, temporarily or permanently, becomes abnormally rich in fat; but the deposition of fat as a *secretory process* only takes place in fatty tissue already formed, or through the growth of new tissue. When the fat cells absorb lipogenous material from the blood as it flows by, and work it up into fat, they are physiologically quite similar to gland cells; while at certain critical periods they permit the stored-up fat to be consumed and to disappear with a development of heat, thus taking a most essential and entirely active part in the play of forces and interchange of matter throughout the whole body. They, in fact, constantly abstract from the mass of pabulum in times of plenty a greater or smaller quantity of valuable material, capable of being employed in the development of force (production of heat), that, like good housekeepers, they may save it up until it can be given out again in time of want, and employed as it is most required.

According to another essentially different view (Virchow's), which has recently received powerful support from the exhaustive researches of Flemming (l. c.), there is no primary distinction between fatty tissue and ordinary loose connective tissue, and the fat cells are, in fact, identical with the regular connective-tissue cells. Any connective-tissue cell, in fact, any cell of any kind, may be transformed into a fat cell by absorption of fat; under ordinary circumstances, however, and even in the less pronounced cases of pathological corpulence, it is only certain loose connective tissue-cells whose situation, as regards the blood stream, specially favors their infiltration with fat, that permanently become so. The blood stream carries with it, in a free form, a store of lipogenous material, the amount of which depends upon the quantity and composition of the diet, and the wear and tear of the organism. A portion of this is constantly transuding through the walls of the blood-vessels; and an increased quantity flows out where, in consequence of a circumscribed dilatation of the smaller vessels, a considerable retardation of the circulation has occurred. This lipogenous material, which exudes from the blood, settles down outside the vessels in the form of fine adipose particles, and thus supplies the fat which occurs as a normal constituent of the various tissues. Where very great quantities are transuded, as in places where there is a partial dilatation of the vessels, there will be a more considerable deposition of fat, and a more distinct fat infiltration of the tissue cells which lie in the neighborhood and are gifted with power of absorption. This partial dilatation of the vessels can, however, occur easily and frequently only in loosely woven tissues, and most easily in the strata of loose connective tissue, which, therefore, is specially subject to become loaded with fat (*i. e.*, to become fatty tissue). And, further, if a partial dilatation takes place anywhere (in small arteries, veins, or considerable capillaries), the connective tissue of the adventitia of the vessels must always first become infiltrated with fat. We accordingly see, in fact, that the production of the fat-clusters (*Fetttraübchen*) takes place as a completely circumscribed process centrifugally around particular portions of small vessels where the adventitia is found loose and permeated with fine drops of fat. Afterwards these fat drops are taken up by the lining connective-tissue cells of the adventitia, and absorbed into the protoplasm; the transformation of these cells into fat cells being thus brought about. Flemming concludes that this local dilatation does always, in fact, precede the deposition of fat, as a primary change; from the circumstance that in the affected localities numerous wandering cells are likewise to be met with in the adventitia. These latter have no direct bearing upon the tendency to fat-production, but their wandering out of the blood in great numbers, yet within narrow limits, affords a presumption that there has been such a circumscribed but considerable slackening of the circulation, as can only take place when a local dilatation of the vessels occurs.

To whichever of these sharply-opposed opinions concerning the histogenesis of fatty tissue we may adhere, the extremely intimate connection which must be maintained between fatty tissue and the vascular system is clear enough. It is only where a rich vascularization exists that a deposition of fat can take place; tissues ill supplied with vessels never become rich in fat. The fat which occurs in fatty infiltration is, moreover, in the main, according to both theories, to be looked upon not as previously formed in the blood, but as originating when the lipogenous material has left the vessels. According to one hypothesis (Toldt), it originates in the cell-elements of a peculiar tissue (fatty tissue); according to the other (Flemming), in the interstices of the tissue of the adventitia of the vessels simply to be absorbed by the neighboring cells as soon as formed. In each of these possible cases, however, in order to solve the physiological problem of the deposition of fat, and to arrive at a conception of the pathogeny of corpulence in all points logical, we are finally compelled to have recourse to the conjuring up of certain auxiliary conditions which individual and temporary variations in the amount of fat-deposition which takes place help us to determine *in concreto*. No one who holds, with Toldt, the specific nature of the fatty tissue, and considers the deposition of fat a secretory process, will be content with the previously laid down conditions of a copious lipogenesis: "rich diet, diminished trophic and plastic energy of the tissues, deficiency of oxygen in the blood." The *secretory energy* of the fatty tissue, which under similar previous conditions may be very different in different individuals or at different times, must count for something. Just so will the abundance of the fat formation depend in this case upon the *quantity of the already formed fatty tissue*, as well as *its capacity for proliferation*. On the other hand, any one who denies, with Flemming, the specific nature of the fatty tissue, and follows him in his further conceptions, must again account for the differences which exist in particular cases by the variable action of the contractile vessel-walls. Vaso-motor innervation and proper irritability of the tissue of the vessels have their part in the question of the more or less frequent occurrence of local dilatation of the vessels of the wide-meshed connective tissue, and therefore of the amount of the tendency to fat deposition. The richness in cells of the adventitia of the vessels and the capacity for development of these cell-elements must likewise be considered. We see, then, that the physiological process of fat-production is really a most complicated one; neither the *magnitude* of the individual factors which conduce to determine the intensity of this fat-production, nor the *nature* of all these factors themselves, being sufficiently known to us to enable us to state the problem, offhand, in exact mathematical form. It has a certain resemblance to many unrelated variables. Under these circumstances it is the less strange that the *pathogeny of corpulence* should, in so many cases of the malady (we may even say in every case), still leave us to grope in darkness which is at first not to be dissipated; and that we accordingly find those etiological forces, under the influence of which, in all common experience, the affection most frequently arises, in many cases either absent or nearly so. However clear, therefore, up to a certain point, the history of the origin of the disease may appear, where the common and more intelligible etiological conditions distinctly coincide, every physician who has any considerable material to arrange must find that cases of corpulence crop up here and there, which, as regards their mode of origin, distinctly bear the stamp of mystery and *apparent spontaneity.* So much for the understanding of the following remarks on etiology, which cannot, of course, claim to be at all exhaustive.

Before we ourselves enter upon an enumeration of the known causes of corpulence, one point, already touched upon in the general introduction, requires special discussion here. We allude to the regular coincidence between the *more intense infiltration of the tela adiposa* (or of the fat-containing connective tissue) with new-formation of this tissue, during the process of normal as of abnormal fat-production. Not only is the magnitude of the individual fat-containing elements increased by greater distention, but they reproduce themselves. The more corpulent the body, the greater the quantity of their elements. According to the theory of Flemming (when we represent it to our minds in its details), this coincidence has nothing strange in it, since, according to him, the more favorable the conditions for fat-deposition the greater will be the quantity of loose connective tissue which must be changed into fat-infiltrated tissue (fatty tissue). It is not right, however, on this account to give the preference *à priori* to Flemming's opinion, since the contrary view of Toldt may be made to harmonize with this fact without difficulty. For if the fatty tissue constitute, as Toldt assumes, a specific form of tissue—which, like that of the glands themselves, is active in the process of fat-infiltration—hyperplasia of this active tissue occurs at times of increased activity, which is analogous to the hyperplasia of glands in continual functional activity, and indeed to the hyperplasia of working muscles, and by virtue of these analogies ceases to be something quite particular and isolated. We must, therefore, since we cannot approach the answer to the question as to the nature and importance of the fatty tissue any nearer chemically, abandon it altogether to the professed histologist, and in our interpretation of the etiological conditions and of the symptoms of corpulence leave it aside as far as this can possibly be done without detriment to that completeness of statement which we desire.

How far this is possible in dealing with the etiology, and in what way it is not possible, the following exposition will show.

Etiology.

(a.) *Predisposing Forces.*

The disposition to corpulence is an extremely variable thing. Under the very same dietary conditions, and under external circumstances in other respects the very same, we see certain individuals remain thin, while others become fat, even to a morbid degree. And when we consider how complex the process of fat-production is, and how many forces conspire to determine the extent of this physiological function, this difference in the individual tendency to corpulence has nothing logically mysterious in it, especially as a number of these factors lie in the inmost recesses of the sphere of somatic organization, so as to be for the most part unconnected with external surroundings. (*See what goes before.*)

We cannot, therefore, do more in the way of explaining the fact of this difference in individual predisposition to corpulence than merely to name the most important predisposing influences, analyzing as far as possible their *modus operandi.* Empirically the following personal conditions are found to occur most frequently in the etiology of individual cases:

1. *Heredity.*—The tendency to corpulence is, in very many cases, an *inherited*, or at least a *congenital* one. We should, indeed, not forget that when the affection develops itself for the first time late in life and among many members of the same family, the external mode of life of these persons is frequently similar, and may favor the invasion of corpulence. But the very most important and most frequent of these external determining causes (immoderate indulgence in food, and a lazy habit of life) here produce injurious results to which numerous individuals of other families expose themselves by living in identically the same way, without suffering from a similar tendency to fat, or at least to an equal extent. Besides this the tendency to corpulence often enough makes itself felt in individuals belonging to such predisposed families yet leading widely differing lives. It is therefore plain that in such cases of the disease some deeper cause must exist, which depends upon a family tendency, and which accounts for the occurrence, in all grades of society, high and low, of groups of individuals who, over and above their blood-relationship, are connected by the common blazon of a pot-belly.

The hereditary tendency to corpulence frequently appears soon after birth, in the first years of life, much less frequently in later childhood, or at puberty; but it most frequently first shows itself in the decline of life, soon after forty, or in later years. It is favorable to the theory of the hereditary transmission of corpulence that it usually exhibits a character which we have already (p. 264) noticed as a common peculiarity of hereditary anomalies of constitution—the fact, namely, that it is most frequently only the *tendency* to the affection which is transmitted. It usually appears distinctly only *with time*—that is to say, at those periods of life which it specially prefers. Whether the sex of children has any influence upon the heredity of the disease is not clearly determined; and just as little, whether it is most frequently transmitted from the father's or mother's side. Our personal opinion is, indeed, that corpulence more frequently descends through similar sexes (from father to son and from mother to daughter); yet we have nowhere in literature been able to find positive data on this subject.

If we ask upon what peculiarity of constitution this inherited corpulence can depend, we naturally refer to those somatic conditions which, on the one hand, influence the extent of the tendency to fat-production (see "Pathogeny,") and on the other hand, possibly or certainly, come under the influence of the hereditary principle. Amongst these we may perhaps specially mention: a. *Hereditary differences in the rapidity of blood-formation* dependent upon *the new-growth of the red blood-corpuscles.* In any individual the slower the continual regeneration of the blood-tissue, and consequently the greater the congenital *hypoplasia of the blood-corpuscles* (see the chap. on Chlorosis), the greater must evidently also be, *cæteris paribus,* the congenital disposition to corpulence, since the habitual amount of oxygenation of the blood is very essentially influenced by the habitual energy of the cytogenic function, while a slight oxygenation is favorable to fat-production (see p. 308). b. *Hereditary differences* in *the trophic and plastic energy of the other tissues of the body,* or even of any specially important tissues, the amount of the deposition of organic albumen being determined by this energy. Individuals whose albumenized tissues, either *en masse* or at least in some of their most important representatives (muscular-tissue, glandular-tissue), possess, from the cradle, a strong tendency to increase and a brisk power of nutrition, require for the satisfaction of this cellular want a greater quantity of nutriment, and are, therefore, much less liable to become corpulent than others who possess a relaxed constitution as an heirloom (see p. 306). c. *Hereditary differences in the quantity, function, and proliferating capacity of the fat-carrying connective tissue and its vascular apparatus.* As long as the peculiar histological nature of the fatty tissue remains undetermined with any final validity, and further, as long as the profound controversies concerning the *modus* of fat-production and fat-development, as we have already described them, continue, it will be best provisionally to avoid the more special formulization of the hereditary differences which here exist. We may, moreover, be all the more content with an hypothesis, for which, indeed, we surely have some grounds, since hereditary transmission may possibly manifest itself in certain circumstances in this histological region also, and become a predisposing cause of corpulence.

2. *Period of Life.*—The predisposing influence of the period of life shows itself most frequently in hereditary cases, but also not unfrequently in those in which no hereditary transmission is demonstrable. It is, therefore, a very decided one; by which we do not mean in any wise to imply that examples of abnormal and morbid development of fat do not occasionally present themselves at other periods of life than those which especially favor this. As we have already mentioned, in speaking of the influence

of heredity, the periods specially favorable to the disease are: the first years of life—the period of suckling; and, in a far higher degree, the period after forty years of age. The later years of childhood, and the period of adolescence, on the other hand, are least favorable to it.

In girls, however, at puberty, under the influence of a long-continued chlorosis, a moderate degree of corpulence not unfrequently occurs. This we have already (see p. 535) pointed out to be closely connected with the chlorosis, and has but little to do with the period of life. With the exception of cases here and there, in which some other predisposing or determining forces induce the occurrence of corpulence at unusual periods of life, we may hold to the general proposition that the overwhelming majority of all cases of morbid corpulence, outside of the tenderest years of childhood, belong to the decline of life.

If we inquire into the deeper grounds of this peculiarity of the disease, we find that these are very different in children at the breast from those that exist in other individuals. It may indeed be confidently asserted that *the polysarkia of very young children* has nothing directly to do with the kinds of chemico-physiological activity (Stoffbewegung) which specially belongs to this period of life, but must be looked upon rather as an accidental pathological phenomenon which has its root in other conditions; for the mode of tissue-change (Stoffumsatz) specially operant at this period, as such, tends, as we know, to the rapid growth of the body (the very great deposition of organized albumen), and therefore works directly against the production of fat.

When, therefore, in spite of this, fat is often produced in astonishing quantity at this age, it can only depend upon some other accident frequently present. Now, we can easily understand why, when a hereditary tendency to adiposity exists (from any of the causes mentioned in paragraph one), the affection should be so much more frequent and regular during the period of lactation than in later childhood and at puberty. We must remember, *first*, that the ordinary food of sucklings—milk—from its chemical composition furnishes a diet specially adapted for fat-production, and that when plentifully given, can, notwithstanding the rapid growth of the body, easily afford opportunity for the production of a corpulent habit, and, *secondly*, that in this earliest period those continual brisk movements of the body, which later, when the child has learned to walk, very materially counteract the production of fat, are wanting (see, respecting this, observations on determining causes a little farther on). This rich and exclusive milk-diet, with deficient action of the muscles, tends, as we know, to produce in healthy sucklings that pretty roundness of the limbs which we like to see, and which afterwards disappears when (in the second year) the food is of a less fat-producing nature, and the numerous motions of the body greatly accelerate molecular change. Where a hereditary tendency to adiposity exists, the very same diet and conditions tend to provoke the development of the disease at the period of lactation. The danger is evidently all the greater when sucklings with a hereditary tendency to corpulence are *improperly* fed, that is to say, on a diet either *too concentrated* or *badly prepared*, which acts as a direct auxiliary to fat-production. We, accordingly, more frequently meet with polysarkia in children fed on concentrated substitutes for milk, such as *Liebig's Soup*, or *Nestle's Infant's Food*, than in those brought up at the breast of the mother or a good nurse. It occurs if these preparations, excellent in themselves, be not carefully adapted, in quantity and concentration, to the idiosyncrasy and period of development of the child, but given in an immoderate quantity and of a pasty consistence. If, finally, *bad* substitutes for milk be used—such as rusk-pap, gruel, etc., which do not furnish a sufficient quantity of inorganic substances (iron, potash, phosphates) required for blood-formation, and if these unsuitable substitutes be given and assimilated in large quantities, instead of the natural food, this irrational diet is pretty sure to induce simply a production of fat, at the expense of the normal formation of blood, bone, and muscle. In such a case corpulence frequently appears as an acquired disease, even in children who probably had no particular tendency to polysarkia at first; since this last-mentioned cause often enough produces what is, strictly speaking, simply an artificial condition, which has so important a bearing upon the period of life at present under consideration only because experience proves that it is precisely at this period of lactation that such sins with regard to children's diet are, knowingly or unknowingly, most frequently committed.

Of that other, and much more frequent form of the malady, which, overleaping not only the years of childhood but those of adolescence and maturity, first shows itself in the period of physiological decadence, that is to say, in persons who have passed their fortieth year, the pathogeny is quite different. This also is, indeed, often enough the product of hereditary predisposition, and is moreover frequently provoked or at least encouraged, in individual cases, by an unsuitable mode of life; but undoubtedly the period of life itself—that is to say, the species of *chemico-physiological activity* (Stoffbewegung) peculiar to it—always plays a most important part in the complex etiological force. Referring to our remarks upon the etiology of anæmia (p. 303), we may remember that with advancing age the organic processes of growth relax more and more, that the tendency of the tissues to secrete organized albumen from that of the pabulum becomes always less, and that further the physiological renovation of the red blood-corpuscles gradually decreases. We may, then, consider that in this lessening of the plastic energy of all the tissues, as well as in the *oligocythæmia*, we have a force predisposing to richer fat-production. How powerful the influence of the period of life in conjunction with that of heredity may prove, is shown by this among other things, that in individuals with congenital tendency to the disease, the occurrence of the critical epoch is frequently, spite of all precautions against his insidious foe, alone sufficient to destroy his youthful slenderness and to confound all the proportions of his figure in a most unpleasant manner.

3. *Sex.*—In the *female* sex, which under physiological conditions exhibits a greater tendency to fat-production than the male, the predisposition to morbid adiposity is likewise a little more decided. This difference appears even in infant life; cases of excessive adiposity being (to judge by the notices in the literature of the subject) much more frequently observed in girls than in boys,[1] the same holds good in the years of adolescence and in

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[1] Among the collected cases of excessive adiposity cited by *J. F. Meckel* (Handbuch

advanced life. It must not, however, be supposed that the number of corpulent persons of the male sex is by any means a small one, or that a veritable Colossus of amplitude is of unfrequent occurrence among them. But it is a well-established fact that corpulence in the *female* sex is much more frequently *apparently spontaneous*—that is to say, is developed without the interference of *external* injurious influences; while in men these influences (excesses in meat and drink, etc.) have comparatively much oftener to be taken into account in the origin of the disease, in addition to the individual tendency. The natural intelligence of the non-medical public, spite of many mistakes in individual cases, is not so far wrong when it fixes upon a corpulent man, without further question, the reproach of an intemperate mode of life; while with a corpulent woman it, on the contrary, is moved simply to a feeling of compassion or a kind of wonder, without asking after any "cause." The greater tendency to fat, both physiological and pathological, in the female sex arises chiefly from the comparative poverty of the blood in the colored constituents (oxygen-carriers) and the less perfect combustion of the non-azotized products of the decomposition of the albumen of the pabulum (see p. 297). We have, moreover, grounds for supposing that the female organism, certain periods (pregnancy) and organs (uterus) being excepted, is on the whole less disposed to the increase of its tissue, or the deposition of organized albumen; and that further this comparative deficiency in plastic energy is especially well-marked in the highly albumenized muscular tissue. Men are, therefore, under more favorable conditions for the production of flesh; while in women more fat is developed from the albumen of the pabulum. Finally, for plain evidence that the fair sex is more rich in fat and more disposed to corpulence than the other, we need only remember that the local development of that "loose connective tissue" (lockere Bindegewebe) which, according to some (Toldt), specially *excites* and to others (Flemming) specially predisposes to the deposition of fat (see "Pathogeny"), is present in women from the beginning in certain regions (fat cushions of the mammæ, the nape of the

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der Path. Anatomie. Leipzig, 1818, pp. 121, 122), there are but two cases (those of *Tulp* and *Clauder*) occurring in boys.

neck, the nates,[1] etc.), in much greater quantity than in men. It is perfectly intelligible why that even rounding of the figure, that softness of outline, which excites such admiration, poetic as well as prosaic, when a woman is in the bloom of youth, more frequently and easily slides into unsymmetrical rotundity and morbid bulk, than the more angular contour of the masculine body, with its greater muscularity. We have, then, in this great predisposition of the female sex to excessive fat-production a further confirmation of the view already expressed by us (p. 266), that *the more easily the dynamic equilibrium of the normal life-processes may be altered in certain directions, the slighter will be the disturbing force necessary to produce a real lesion of health.*

4. *Physiological Constitution.*—As a product of hereditary transmission, as well as of acquired differentiation, the individual form in which, in different persons of similar age and sex, and under similar external circumstances, the functions of life are fulfilled—that is to say, the *physiological constitution* of the individual (see p. 267), is very different as regards the tendency to fat-production, and naturally also different as regards the tendency to morbid corpulence. According to the deductions made in our section on Pathogeny, this tendency will be in almost direct proportion to the richness in lipogenous material (albumen and fat) of the pabulum ; and it follows from this that persons of *plethoric* constitution (full-blooded persons), not merely, as a rule, throw up more fat than most thin-blooded persons, but are also in greater danger of becoming corpulent, *i. e.*, morbidly fat. Yet, on the other hand, in that condition of physiological oligæmia which we speak of as "habitual delicacy," without classing it quite among real diseases (see p. 305), much will depend upon whether the mass of the circulating fluids, and especially the quantity of lipogenous material contained in them, is small or large as compared to the mass of the

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[1] In this connection, the excessive development of fatty tissues in the *nates* of the negresses in some South African races, in whom this produces a regular fatty protuberance in the gluteal region, is of ethnographic interest. Compare the representation of the "Hottentot Venus" in *Luschka*, "Anatomy of the Pelvis," Tübingen, 1864, and the original observations of the author on this circumstance.

red blood-corpuscles—or, in other words, whether in *individuals of delicate constitution hypalbuminosis or oligocythæmia prevails.* In the first case the conditions are evidently *unfavorable* for fat-production, and the affected person will have a weakly appearance (see "Anæmia," p. 309). In the latter a *considerable* amount of adiposity may exist, since from the non-oxygenation of the blood, and in proportion to this, a great quantity of fat may arise from the albumen of the pabulum. Such persons look pale, though bloated, or pasty, and are found to be almost as liable to corpulence as the plethoric. There is, then, *a form of physiological anæmia which predisposes to corpulence; and enormous deposition of fat is by no means invariably a sign of fullness of blood; it is quite as frequently a sign of sluggish blood-formation or relaxed constitution.*

The amount of the red corpuscles depends chiefly, under physiological conditions, as has been already frequently observed, on the rapidity of their regeneration. This latter function, moreover, forms a part of the regenerative process of the whole organism, and manifests those individual differences in their intensity which sometimes (as in chlorotic hypoplasia of the blood; see our chapter on "Chlorosis") occur in an isolated manner, and sometimes may homologously extend to the regenerative and developmental processes of the remaining tissues. We now, of course, speak of constitutions in which the new formation of the blood-tissue goes on comparatively more sluggishly, and in which the trophic and plastic energy of the other tissues is to a similar extent deficient—*relaxed* constitutions (see p. 306), distinguishing them, on the one hand, from the *tough* (sthenic) constitution, and, on the other, from the *irritable* anæmia. Whilst in the latter there is little tendency to corpulence, the relaxed constitution is very much disposed to it, *first,* because the amount of red blood-corpuscles is disproportionately small, and *secondly,* because the tissues have but slight capacity for storing up organized albumen. On the other hand, a corpulent habit with pale countenance is the most important external sign of the relaxed constitution (p. 309).

When the plethoric or the relaxed anæmic constitution is the special product of hereditary transmission, as is often the case, the tendency to corpulence appears as the hereditary idiosyncrasy of the affected person. When, on the contrary, this individual form of constitution is produced in later life in consequence of external circumstances, through the gradual metamorphosis of the original type, there results an adipose proclivity which is evidently an acquired one, and which may have no analogy in the family circle of the affected person. As to the nature of these influences, through which a strong constitution may become in some cases plethoric, in others relaxed, and occasionally predisposed to morbid corpulence, we must here content ourselves with a reference to the *Determining Causes* of Corpulence (see farther on). These latter, when their intensity is but slight, only produce a tendency to adiposity, but in other cases they are capable of producing the disease *immediately* (*i. e.*, without previous predisposition).

5. *Temperament.*—Among the special predisposing causes of corpulence we enumerate since Galen's time, as every one knows, that peculiarity of temperament which is marked by comparative weakness of the passions and affections, and greater emotional stability, and which bears the time-honored appellation of phlegmatic.[1] The choleric has just the opposite reputation as regards fat-production.

This notion of the different influences of temperament upon fat-production is so widespread and so deep-rooted that it is quite common, even to reason back from the greater or less fatness of an individual to his temperament. We, accordingly, are disposed to look upon any fat person we may come across as less disposed to pondering and brooding, and therefore less thoughtful, besides being free from the stronger passions, and therefore even-tempered, and on the whole good-natured. With the notion of uncommon leanness, on the contrary, we involuntarily connect that of restless, profound curiosity, consuming passion, and even uncanny suspicion. It is historically known and poetically endorsed that Julius Cæsar, for instance, disliked to see thin persons near him because he held them as secret enemies and conspirers against his tyranny, while he feared nothing from "men that are fat, sleek-headed men, and such as sleep o' nights,"[2] believing them, not altogether unreasonably, to be politically safe. It cannot be denied that the greater or less energy of the psychical functions, the more or less rapid play of conceptions, moods, and impulses, may influence the rapidity and direction of physical processes on this account at any rate, because the psychical disposition influences in a very perceptible manner the dietary requirements as well as the voluntary activity of the muscles. It will be evident, for instance, that in the man of choleric temperament, every violent impulse which usually finds vent in eager activity will accelerate tissue-change and restrain fat-production. On the other hand, it is intelligible that the phlegmatic temperament which conduces to corporeal sluggishness, but not at the same time to temperance, furnishes external conditions specially favorable to the corpulent habit. But we can scarcely avoid affirming that there exists a still deeper reason for that coincidence between the phlegmatic temperament and adiposity which is so frequent. It is, indeed, extremely probable that both mental disposition and bodily habit must often *have their origin in one and the same root*, the relaxed constitution, or, in other words, that a sluggish and unproductive brain function often corresponds to, and is one of the symptoms of, that sluggishness in the other organic functions, which favors the occurrence of the corpulent habit.

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[1] From one of the four cardinal humors of Galen.

[2] See *Plutarch's* Life of Julius Cæsar, chap. 62, and Life of Marcus Brutus, chap. 8, and also *Shakspeare's* Julius Cæsar, Act I., Scene 2.

Cæsar: Let me have men about me that are fat;
Sleek-headed men, and such as sleep o' nights;
Yond' Cassius has a lean and hungry look;
He thinks too much: such men are dangerous.

In conclusion, we must not omit to say that the influence of temperament on fat-production, highly as it may always be estimated, is yet by no means such a powerful one that there are no exceptions to the rule: idealless, unemotional blockheads who sit upon thin rumps, and, on the other hand, well-fed pot-bellies whose brains are full of lively ideas and burning desires, and who are smart, energetic, enterprising, and often enough even intriguers!

6. *Anomalies of the genital functions.*—A suppression, diminution, or complete absence of the genital functions generally

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Antony: Fear him not, Cæsar, he's not dangerous;
He is a noble Roman, and well given.
Cæsar: 'Would he were fatter: But I fear him not!
Yet if my name were liable to fear,
I do not know the man I should avoid,
So soon as that spare Cassius.

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acts as a force favoring the occurrence of corpulence in the male sex. A life of sexual excesses is, on the other hand, regarded as a frequent cause of excessive thinness and dryness in men; it therefore pleases every one to imagine the rake as "lean." It may be remembered that in the "Etiology of Anæmia" (p. 323) we have explained that, at all events, venereal excesses, by carrying off in the semen a great quantity of rich material, may lead to poverty of blood and marasmus in men. We cannot, however, *at once* admit the converse conclusion that because a certain quantity of fat-producing material remains to be used up in the body, when these losses of nutrient fluid do not take place, complete abstinence and chastity *per se* frequently produce fat. It is certain that while this is, generally speaking, a force tending to produce corpulence, it is one of very inferior importance, since the mass of lipogenous material lost in moderate sexual indulgence can easily be made up by a slight increase in diet. The reasons for the frequent occurrence of corpulence in individuals who have taken the vow of chastity, and who really succeed in keeping it—and of castrates (men or animals), and other unfortunate creatures whose genital development has remained imperfect, are usually elsewhere to be sought. Above all we find that those who have renounced the *best* things of this world are, when they have an opportunity, notorious for sticking fast to its *good* things, often enough taking to the pleasures of the table, in the hope of consoling themselves for the joys of Venus which they have given up. If therefore so many examples of the disease occur in cloisters and monasteries that it is difficult, in the face of this, to imagine an abbot, for instance, as anything but fat, this rotundity of person should be attributed rather to good kitchens, and good cellars, and that quiet contemplation which is the business of life with these worthy celibates, than to their chastity. This, however, does not falsify the observation already made, that the deficiency in the genital function is in other respects favorable to corpulence, and even has decided influence on physiological *embonpoint*. The experience of farmers, indeed, tends to demonstrate clearly that with male animals similarly fed and reared, the castrated (oxen, wethers, capons) fatten much more easily than the uncastrated. The same thing may be affirmed of human eunuchs whose tendency to corpulence even in unfavorable circumstances is notorious. We shall scarcely err, therefore, if we connect this predisposition to corpulence with that general change of constitution which results from early castration, and, as we know, expresses itself in the habit of such persons by other signs. Experience compels us to admit that whether through the blood, or the nervous system, a physiological connection is established between the genitals and other distant parts, that their development depends upon that of the genitals, and that where, after complete castration or in deficient genital development, this impulse is wanting, they (*e. g.*, the larynx, hair of the beard and pubes, etc.) also remain imperfectly developed. Now, it is very probable that the blood-tissue itself forms a part of that element whose development is arrested by the removal or maiming of the sexual function, and that the greater tendency to adiposity, which is empirically observed in castrated animals and men, is the consequence of a functional sleep of the cytogenous apparatus, and of a sluggish hæmatopoiesis ; or, in other words, that it depends on a certain amount of oligocythæmia, which should be regarded as the sad consequence of the attack upon the genital sphere, or the congenital deficiency. Finally, it is not possible to show that castration, performed after sexual maturity has been attained, or a voluntary suppression of the awakened genital function through strict fulfilment of a vow of chastity, necessarily affords even a much slighter impediment to the blood-formation than the nipping of this function in the bud, though acting in a similar manner ; and that therefore the corpulence of religious celibates is probably connected not merely with their vows (see above) but with their duties.

What has been laid down respecting the *male* sex, holds good for the *female* also. We must first remember that the greater predisposition to corpulence in women manifests itself especially in the decline of life, and therefore at a time when the genital function is *in process of extinction*, or already *entirely extinct*. It is further quite intelligible that, apart from causes previously mentioned, which, putting this out of the question, make the female organism more liable to fat-production, the male sex is less predisposed to it in advancing age, because it has not to go through a definite climacteric period, and often preserves a certain amount of sexual ability up to the very latest years of life. The fact that corpulence, with overwhelming frequency, *begins clearly to develop itself just when the menses cease*, and the periodic process of ovulation is discontinued, places the etiological connection between fat-production and deficient genital function in its clearest light. This remarkable fact, which can be empirically demonstrated in numberless cases, is surely just as powerful an argument for the reciprocity between the evidence of sexual activity and fat-production, as the frequency of adiposity in male castrates, and is important as completing our enumeration of the arguments in favor of the theory we have above put forward.

We may further add that in female animals early deprived of their ovaries (castrated hens or so-called pullets for instance), when well fed, an unusual tendency to fat is, as a rule, produced, and that, at all events, the suppression of the genital function results in the female sex in a very much greater retention of lipogenous material than in the male. How much material, for instance, from which the fat of the body might be produced, must be directly lost in the form of eggs in laying hens!

An interesting phenomenon, which may best be noticed in this connection, is the *frequency of sterility* in fat women in the bloom *of their youth.* This, which was known even in antiquity (see "Historic Sketch"), long ago occupied the attention of minds medical and non-medical. Of the fact itself there can be no doubt; but it is more difficult to answer the question whether the sterility is cause or effect of the corpulence, or, finally, as is perhaps in most cases most probable, whether both corpulence and sterility are not co-effects of some deeper cause. If we except cases in which corpulence acts as a mechanical hinderance to impregnation, and is thus a cause of sterility, and those in which, on the other hand, sterility, dependent on other causes (rigidity of the *os uteri*, prolapsus, or chronic catarrh of the uterus, etc.), acts as an auxiliary cause of corpulence by preserving the lipogenous material of the pabulum, it may be that sterility with unseasonable corpulence in a woman usually depends upon a relaxed state of the constitution, especially a plastic weakness of the cytogenous and genital apparatus, which is the fountainhead of both anomalies. Those women whose ovules are weak, deficient in developmental power, and perhaps also small in number, often apparently labor at the same time under a hypoplasia of the red blood-corpuscles which predisposes to fat-production and induces early corpulence. Finally, the same remedies which stimulate hæmatopoiesis, and under certain circumstances (see "Therapeutics") from this property constitute a most important prescription against corpulence, may possibly in many cases be relied upon also to diminish the weakness of the genital apparatus, in such a manner that conception may occur where such a thing could no longer be reckoned upon.

8. *Determining Causes.*

The determining causes of corpulence are partly external, partly internal. There are accordingly idiopathic and symptomatic forms of the affection. As causes of idiopathic corpulence it is usual especially to name:

1. *Intemperance in diet, and the use of spirituous liquors.*—We must consider *excess* in diet the prominent cause of corpulence more frequently than any of those other causes which may also provoke the disease, where there is no original tendency, or in which the period of life, sex, etc., of the affected person do not act as predisposing causes. It will have this determining effect all the more surely when an individual or temporary disposition to corpulence exists, and where it only requires an external impulse to call it into play. The manner in which the various constituents of the diet (albuminous matter, hydrocarbons, gluten, etc.) are concerned in fat-production is more distinctly described in the section on Pathogeny. A simple consideration will, however, show further that the most favorable conditions for rich fat-production in man are afforded when the food is not only very rich, but suitably mixed. Indeed, although the albuminates and homologous fats of the diet are remarkable for their direct lipogenous influence, in omnivorous man a diet confined exclusively to flesh would scarcely be likely to produce corpulence; for, in the first place, it would not be possible for

him to make use of such a monotonous diet for any considerable time without loathing, and, in the second place, the digestive capacity of the stomach, intestines, and pancreas would be incapable of digesting and assimilating a quantity of flesh sufficient to produce any considerable corpulence. We should never forget that the stream of nutrient material which is poured through the gates of the digestive apparatus into the circulating pabulum of the body must supply the deficiency caused by necessary expenditure before it can out of its superfluity lay up a store of organized albumen, or, more than this, of fat. This necessary expenditure involves above all these the requisite production of heat and a certain quantity of muscular work (movements of the heart and lungs) which *per se* absorb so great a quantity of non-azotized material that it is only when there is an extremely large assimilation of albumen, and an excessive destruction of this albumen of the diet, that any great quantity of fat can be secreted and stored up unconsumed. The conditions are much more favorable with a mixed diet in which, together with a great quantity of albumen, there is plenty of fat, starch, sugar, and gluten. Such a mixed diet admits of much greater variety, and is therefore much more palatable. It is besides more easily and completely digested, and therefore goes farther in supplying the wants of the organism. It moreover permits the body to obtain the means for necessary expenditure almost entirely from the other nutrient elements, and therefore in the most distinct manner gives an impulse to the storing up of organized albumen, and, indeed, of fat. We therefore find that, except in the case of sucklings who are too richly or improperly fed, morbid corpulence is most frequent in those easy-going *bon-vivants*, to whom eating is an end in itself, and on the variety as well as the fullness of whose meals it therefore depends. The richness and variety of their daily *menu*, on the drawing up of which they expend such labor, permits them, on the whole, to eat far more than those who have a less number of courses desire to eat, or ever eat, and furnishes them with nutrient material not only in larger quantity, but in an admixture especially favorable to the production of corpulence. Corpulence, indeed, develops itself very often in those "public men"

—"men of the day," who, on account of their national, artistic, literary, or social labors, etc., etc., find themselves "compelled" to assist as prominent guests at all sorts of feasts, banquets of honor, etc., and who therefore, without being actual *gourmands*, must frequently perform astounding feats in the eating line for the honor of their "loftier aims," and, as we know, may easily come to look upon the doughty deeds of their mouths and stomachs as great achievements in the spheres of sentiment and intellect. That many of these pillars of our modern commonwealth should by this voluptuous mode of life develop rather corporeally in breadth than intellectually in height, is surely no wonder—all the less since while eating they no more forget to drink than professional connoisseurs.

The favorable influence of alcohol upon fat-production reveals itself in the fact that it for the most part undergoes combustion in the body, thus absorbing oxygen in great quantities, and so hindering the combustion of the formed and stored-up fat. *The copious use of alcohol, and especially its use in a concentrated form, is therefore a very frequent cause of corpulence.* Dram-drinkers, for instance, while their digestion remains but slightly impaired, are recognizable by their considerable padding of fat, and their faces frequently have that well-known bloated look which is so repulsive. Wine-drinkers are similarly exposed to the danger of becoming corpulent (though in a less degree), especially if they are fond of drinking strong wines or sweet kinds (like champagne), or if what is lacking in concentration is made up for by quantity. Professional beer-drinkers, finally, almost always take their beloved drink in such large doses that they not only consume in the long run a great deal of alcohol, but also a quantity of sugar of malt, dextrine, etc.—in short, an enormous amount of hydrocarbons, and thus afford their *panniculus adiposus* a double opportunity for storing up fat. Among our academic youth, for instance, accustomed as they are to beer-drinking jollifications, although their age is not such as favors the disease, untimely corpulence is no unfrequent phenomenon. The old *habitués* (Stamm-Gäste) of the "*Brauereien*"—whether they assemble daily at the same table merely for the love of the beer, or for some other object which rejoices the heart of man—are also known to furnish a remarkably strong contingent to the ranks of the corpulent.

2. *Insufficiency of bodily activity.*—The farmers, whose occupation it is to fatten cattle, have long since known that a beast which is to be quickly fattened by good feeding should not work, or even move much. Just so the favorable influence of rest, sluggish mode of life, etc., upon corpulence in the human subject was known to the ancients (see Historic Sketch), this knowledge being the basis of many curious theories in the Greek system of education. Several circumstances apparently work together to make a considerable amount of bodily motion act as a preventive to corpulence, and a sedentary life, with little exercise, a powerful auxiliary to it. Here we may observe that it is an almost universal physiological rule that tissues which function strongly are also inclined to increase their integral organic constituents, or, in other words, that an intense excitement is generally followed by a more intense nutritive and plastic excitement. Thus, glands are, as we know, hypertrophied through strong and continued action, and muscles methodically exercised increase very considerably, and comparatively very quickly, in mass and circumference, through the absorption of organized albumen. *Suitable bodily exercise, with good feeding, is therefore a very appropriate means of putting up flesh.* On the other hand, the quantity of urea eliminated even in great muscular activity is not materially increased (Voit); whence it may be concluded *that the decomposition of the albumen of the pabulum is not essentially accelerated by mechanical efforts.* Now, as fat can arise from the albumen of the pabulum only by a process of decomposition, violent bodily exertion can favor the production of fat from the albumen only in an almost imperceptible degree. Moreover, we may hence deduce the conclusion that, with similar quantities of food, the more organized albumen passes into the voluntary muscles in consequence of their increased activity, the smaller will be the quantity of fat which arises from the albumen of the pabulum. *Increased muscular action therefore lessens the tendency to fat-production, because it favors the production of flesh; bodily rest, on the contrary, favors fat-production,*

by antagonizing the production of flesh; but, more than this, in the contraction of muscle, as we know, besides other products of the decomposition of the complex muscular substance, carbonic acid is produced, so that in increased muscular action a quantity of this gas must be developed in the blood, which, in its turn, induces an acceleration and deepening of the breathing; but, when this becomes intenser and more frequent, the acidity of the blood becomes considerably greater by the absorption of oxygen, and that portion of the excess of oxygen taken up, which does not serve for the synthesis of the unoxidized substance in the muscles (see p. 381), will take possession of the non-azotized consumable material of the pabulum, and turn it into carbonic acid and water. Bodily exertion, then, counteracts the formation of fat, because, in consequence of it, more oxygen is taken up, and more non-azotized material is burnt away into carbonic acid and water. On the other hand, slothful inactivity is favorable to fat-production, because it decreases the energy of the respiratory process, diminishes the oxidation of the blood, and permits the burning-off of non-azotized material in carbonic acid and water only in a diminished degree. *In violent voluntary motions of the body, not only will less fat be produced, but, owing to the more energetic process of oxidation in the tissues, more lipogenous material will be destroyed;* on the contrary, *in long-continued bodily rest more fat will be produced, and less lipogenous material will be destroyed.* Since both processes, in both ways, exercise a similar influence upon the amount of the tendency to fat-production, it is easy to see that the variable condition of the muscular function is a constant and extremely important factor in the amount of fat-production, and that it is not right to estimate the amount of fat-production exclusively by the absolute amount of food assimilated.

3. *Certain morbid processes*, finally, are calculated to produce corpulence *symptomatically* and as a *sequela.* We may once more here mention *chlorosis*, and must refer to our observations (p. 534) on development of corpulence from this cause. Similarly, in *progressive pernicious anæmia*, unusual corpulence has been observed post-mortem (Biermer, Immermann). In those

cases, however, it remained doubtful whether this had originated at an earlier period, or had been first developed in the course of the anæmia. It is known that sometimes, *after copious loss of blood*, corpulence may occur with high feeding (Stark,[1] J. Bauer[2]). The latter author specially mentions an analogy to this clinical experience, that frequent blood-letting, with good stall-feeding, is a good method of producing the greatest possible amount of fattening in herbivorous animals, and that experienced farmers have been accustomed to practise it from time immemorial. In all these cases the poverty of the blood in hæmoglobin, whether of pathological origin or artificially produced, undoubtedly plays a most important part in the genesis of corpulence, which is further promoted by the slight oxidization of the blood. Averbeck[3] mentions, moreover, in his characteristics of the *morbus Addisonii*, that the bodies of those who have died of this disease, as Addison had already found to be the case, are frequently characterized by extraordinary fatness. If the opinion be true that the severe clinical phenomena in the disease depend upon a lesion of blood-distribution, in which, through vaso-motor paralysis in the territory of the splanchnics, a considerable hyperæmia of all the organs of the abdomen, with great anæmia of all the regions of the body, is developed, the injury to the circulation of the lungs would here also prove an active force in preventing oxidation of the blood and producing a tendency to fat, which the anatomical condition of the *tela adiposa* would reveal pathologically. For the rest, we avoid entering more particularly into the essence and developmental history of this interesting affection, and on this point refer the reader to Vol. VIII. of this handbook. Finally, the tendency to corpulence in those diseases of the heart and lungs which lead to a hinderance to the circulation in the respiratory organs, depends upon a deficient supply of oxygen. That this tendency does not more frequently result in really well-marked corpulence is due to the fact that these diseases are generally complicated with lesions of digestion, and also at some period of their course with febrile symptoms, thus involving conditions which directly antagonize the corpulent habit.

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[1] L. c., p. 285.

[2] L. c., p. 599.

[3] Die Addison'sche Krankheit. Erlangen, 1869. p. 30.

Pathology.

General Aspect of the Disease.

The commencement of the disease, when it occurs in adults, and especially elderly individuals, is almost always slow and gradual. In cases of this kind the morbid putting up of fat very rarely takes place rapidly, within a few weeks. With sucklings, on the contrary, a subacute commencement is usually observed ; and those cases, in which in young individuals this lesion of general nutrition occurs symptomatically, after loss of blood, or as a consequence of chlorosis, etc., also seem to develop more rapidly. The most perceptible alterations affect the external habit, which, as is well known, becomes fuller and rounder, and of which the contours extend more and more in breadth. In the countenance this fullness is especially imprinted on the cheeks, which usually not only press the lower eyelids upwards and diminish the space between the lids, but finally also, in consequence of their increase in volume and weight, hang down in the form of huge sacks overshadowing the upper part of the neck, and, as so-called collops (Hängebacken), give the face a particularly foolish expression. A further anomaly occurs in the face through hyper-development of the submental fat—namely, the so called double-chin—a broad tumor of the skin richly stuffed with fat, which gradually spreads from below around the true chin, which is less rich in fat, and seems at last to be hidden altogether behind this excrescence.

In contradistinction to the aforesaid portions of the face and upper part of the neck, the skin of the hairy scalp and the forehead, the eyelids, the muscles of the ear and the nose—in brief, the skin in those places where it is more tightly bound to the underlying soft parts, and is less movable, shows no increase in volume, or at least very little. On the other hand, the deposition of fat is greater in the region of the neck, so that the length of this portion of the body appears remarkably shortened. Indeed, the illusion may occur that the short, thick neck has almost altogether disappeared between the fat face and the no less fat trunk. The fat padding reaches its maximum in the thorax, in the retro-mammary fat-tissue, producing in both sexes, especially of course in the female, an enormous increase in the circumference and volume of the breasts, between which the sternal portion, poor in fat, runs like a narrow, deep, longitudinal valley. From the weight of this fat cushion of the mammary glands it further comes, as a rule, to hang down and cover both hypochondriac regions, in which case the breasts are separated by a deep fold from the belly which extends beneath them. As the common covering of both sides and back of the thorax is usually densely infiltrated with fat, the intercostal spaces appear in consequence to be filled up, the spinal processes scarcely, if at all, prominent, and the skin, wherever one tries to pinch it up into folds, uncommonly thick and voluminous. This takes place even to a much greater extent in the anterior abdominal wall. Here in corpulent people the external fat of the body generally attains its most remarkable and often quite enormous development, thus producing that well-known typical form of "paunch" or pot-belly," in comparison with whose balloon-like circumference and pretentious dimensions, in a well-marked case of the disease, the volume of all other parts of the body appears but small. On the height of this mighty projection the almost invisible navel lies hid in front, generally deeply imbedded in the exuberant fat-cushion which encloses it on all sides. The same holds good of the external genitals, of which the subcutaneous stratum remains almost free from fat in both sexes; not only because of the overhanging vault of the belly, which frequently entirely prevents their possessor from inspecting them, but also from their modest retirement in the midst of their fatty surroundings (mons veneris and upper part of the thigh) which makes them less exposed than formerly to the gaze of other observers. The skin of the inguinal region, moreover, forms the bottom of a deep furrow, of which the voluminous side-tumors are formed by the enormously fat belly and skin of the upper part of the thigh. Behind there is a similar deep boundary line between the upper thigh and the buttocks, strongly and distinctly marked on both sides, the bottom of which is usually completely concealed by the overhanging parts in the neighborhood. The gluteal region is, next to the anterior wall of the abdomen, the region of the body in which the external deposition of fat in pathological adiposity is thickest; the buttocks on this account appear in every direction unusually large, and, like the fat-padding in the *regio mesogastrica*, overhanging, but at the same time much rounded, and of tense, elastic consistence. If we further imagine a considerable augmentation in the volume of both extremities, viz., great fat-cushions on the shoulders, the inner surface of the upper arms, the backs of the hands, and upon the inner surface of the upper thigh, calves of the legs, backs of the feet, and complete the picture thus presented with deeply-cut furrows in the skin at the bends of the elbows and knees, wrists and ankles, produced by the projecting tissues in the *parts richer in fat*, and groove-like retractions at the zones *poorer in fat*—and this over the entire surface of the body—we have a pretty correct conception of the external configuration of a corpulent patient. This is in fact an expression of that portion of the symptomatology of corpulence which is most perceptible to the senses.

That increase in thickness of the general surface which may easily be perceived by inspection and palpation further influences characteristically the phenomena of percussion and auscultation over the thorax and abdomen. The percussion-sound wherever air-containing parts (lungs, stomach, and intestines) underlie the external surface of the body is masked, if not completely dulled. Over the abdomen, meanwhile, this masking may, by reason of the simultaneous fat-infiltration of the subcutaneous layer of the *omentum majus* in well-marked cases of the disease, reach such a pitch that it appears almost completely dull; so that it is only by pushing the disk of the pleximeter deeply into the abdominal surface and by strong percussion with the hammer that it is possible to educe the clear sound of the stomach and intestines. It is further interesting that in many cases of corpulence in which an extreme fat-infiltration of the mediastinal cellular-tissue has occurred, there is, besides the heart's dullness, a masking of the sound over the sternum, and extending on both sides of it, which is referable to the deposition of fat, and is not the physical expression of any abnormal change of grave import (thickening of the anterior margins of the lungs, mediastinal tumors, aneurism of the ascending aorta, etc.). In correspondence with this masking of the percussion-sound over the lungs, we find also upon auscultation the respiratory murmur much slighter and less easily heard than it is in thin individuals. In this manner the heart's sounds are in many cases weakened and perceptible only with difficulty ; though as to this it must be remarked that numerous exceptions to this rule occur, in which the heart's sounds are comparatively very loud and even sharply accentuated (klappend). The reason of this phenomenon is to be found in the frequent presence of hypertrophy of the left side of the heart in corpulent persons, which naturally must have a contrary influence on the distinctness of the auscultatory phenomenon from that produced by the increase in the thickness of the wall of the thorax (see, concerning this point, farther on). The increase of the external and internal fat of the body finally expresses itself in a gross physical manner in a corresponding increase in weight. This, under certain circumstances, may attain to a colossal degree, exceeding the average weight of healthy persons of like ages three or four fold. This excess of bodily weight is naturally most conspicuous in corpulent children, and we may adduce here, for curiosity's sake, a few examples of this which we have now before our eyes :

Boy aged 1¼ years (observer, Barkhausen. Hannov. Annalen. Band III. 2. 1843.)	53 Pounds.
Girl aged 3½ years (observer, Heyfelder. Med. Zeitschrift des Ver. f. Heilkunde in Preussen. 1834.)	(German.) 49½ Pounds.
Boy aged 4 years (observer, Tilesius. Vogt's Magaz. Bd. V. p. 289.)	33 Pounds.
Girl aged 4 years (observer, Kaestner. Hamburg Mag. Bd. II. p. 356.)	82 Pounds.
Girl aged 4 years (observer, Benzenberg. Vogt's Mag. Bd. VI. p. 251.)	137 Pounds.
Boy aged 5 years (observer, Tulpius. Obs. Med. Lib. III. cap. LV. p. 269.)	150 Pounds.
Girl aged 10 years (observer, Eschenmayer, Tübinger Blätter, 1815. Bd. I. p. 261.)	219 Pounds.

The most celebrated example of excessive weight in a corpulent *adult* is that of the Englishman, Ed. Bright, who weighed 609 pounds (Phil. Transactions, Vol.

XLVII., p. 188). William Banting weighed, when he undertook the experiments which bear his name, only 202 lbs., his height being five feet five inches. This was, however, 62 lbs. more than the average corresponding to his height (l. c.). Examples (taken from former times) of unusual corpulence in adults, with reports of their weights, are to be found in Quelmalz (l. c.). From our own observations we may in conclusion bring forward one case in which a corpulent woman, 46 years old, weighed 324 lbs.

The general aspect of corpulent individuals in other respects is marked in certain cases by not inconsiderable differences of practical importance (see "Therapeutics"). The difference between *two typical forms of corpulence*, between which many intervening species of undecided nature exist, is moreover not without essential inductive importance as regards the deeper understanding of the genesis of our disease. We can describe these two typical forms of the disease, under which by far the greater number of all well-marked cases may easily be ranged, according to the probable condition of the general nutritive process, as 1*st*. the *plethoric*, and 2*d*. the *anæmic*.

In pure cases of plethoric corpulence, as they most frequently occur in men in middle and more advanced life, the visible surface of the body, and especially the skin of the face, the mucous membrane of the lips, etc., is unusually vividly and strongly injected, and therefore very red, the arterial pulsation full and tense, the venous system of the skin also strongly filled, and the heart's impulse, finally, bounding and often dislocated downwards and outwards. The physical phenomena of the vascular apparatus point therefore to an unusual largeness of the volume of the blood (polyhæmia), and often at the same time to a hypertrophy of the left side of the heart, but *not* to primary and absolute oligocythæmia. As a contrast to the picture thus drawn, the pure cases of corpulence of an *anæmic* type (more frequent in women), besides the great development of the fat of the body, are characterized by a very distinct pallor of the skin, the lips and visible portions of the mucous membrane being slightly injected, the arterial pulse small and weak, the heart's impulse scarcely distinguishable; and, finally, the general conditions of the cardiac dullness and the remaining physical phenomena as regards the heart in no way point to hypertrophy, but usually to almost normal size or to atonic dilatation of that organ. The great tendency to faintness which distinguishes these cases of corpulence from the others, is connected with this habitual weakness of the heart's action. In short, were it not for the great tendency to fat-production perceptible in both, we should scarcely feel tempted to refer these well-marked cases of anæmic and those of distinctly plethoric corpulence to one and the same morbid species in a pathological system. Between these, however, as has been already remarked, lie not a few cases, of which the shades of difference are very slight, and which it is therefore difficult to bring under one category or the other, either because the corpulence and the general symptoms that accompany it are at first only present in a rudimentary condition, or because, when the disease is pronounced, the color of the patient may appear expressive of anæmic corpulence, while the phenomena of the pulse and heart point on the other hand rather to the plethoric type. While, therefore, in *well-expressed* cases of purely anæmic corpulence, we cannot conclude from the phenomena of the circulation that there is an increase in the volume of the blood, while there is instead *a poverty of the blood in red corpuscles*, with normal or even diminished quantity of blood, in *well-expressed cases of a hybrid character* we are almost bound to admit the conception of a *relative oligocythæmia* (the so-called *serous plethora*). To complete this account we may add in conclusion that many cases, originally of a plethoric character, after a while gradually pass into the anæmic form.

Such a change is especially common in the corpulence of advanced life, less frequent in the plethoric corpulence of small children and youthful individuals. It announces itself by a change of complexion, and those well-known circulatory symptoms which, as we have described them before, need not here be further dilated upon.

The *pure* forms of plethoric as of anæmic corpulence, with many generic peculiarities, usually exhibit differences one from another from an *etiological* point of view. To the common etiological characteristics belong more especially their occurrence as hereditary, and also, in other cases of both kinds, as non-hereditary affections; and their occurrence in both sexes and at all ages—naturally prevailing particularly at those periods already mentioned (the period of suckling, of physiological involution, and of advanced life). Anæmic corpulence is, however, more frequently than plethoric an hereditary affection, and is much more prevalent in the female sex (see above).

Now, since the absolute frequency of hereditary cases exceeds that of non-hereditary, and the tendency to the disease is greater in the female sex, it follows that the majority of all well-marked cases of corpulence belong to the anæmic type. On the other hand, plethoric corpulence more frequently occurs in the less predisposed male sex (see above), and the latter type of the disease develops itself oftener without palpable heredity, under the influence of distinct determining injurious habits. Among these latter, intemperance in eating, and abuse of alcoholic beverages most frequently lead to the plethoric, while sluggish quietude of the body and the morbid processes already mentioned (p. 647), which have symptomatic corpulence for a consequence, most frequently induce the anæmic form of the disease. For the production of hybrid cases, finally, many anæmia-inducing causes, such as deficient bodily activity, may combine with those which usually produce a *plethora sanguinis*, such as alcoholism, gluttony, etc. As to the relative frequency of the two principal forms of corpulence in the different periods of life in the male and female sexes, no essential variations in point of time can be admitted. In other words, the corpulence of the period of suckling, as of that of youth, and of more advanced age, reverts to its constant type in both sexes, principally, if not exclusively, according to the peculiar predisposition of each sex, the differences of which, as we have already seen, have their ground partly in the inner conditions of the individual, and partly in their external accidental conditions of life.

Now, as a general rule, as one or the other type of the disease clearly expresses itself through the complexion of the corpulent individual as in the characters of his cardiac action, other definite symptoms, general as well as local, usually prevail. Patients with *plethoric* corpulence exhibit, as a general rule, a *much better developed muscular system*, a *brisker appetite*, and a *better digestion.*

It is even the rule that with them the demand for food remains for a long time keen, and the digestive functions excellent; and that the patients, therefore, continually fall into those old sins of intemperance which so frequently in these cases have given the principal impulse to the disease. In patients with anæmic corpulence, on the other hand, the *voluntary muscular apparatus* is usually very *deficiently* developed, the appetite bad, or *capriciously perverse*, and less disposed to relish meat and other specially hæmatogenous articles of diet, or the starches, milk, fat, etc., the digestion giving every sign of *atonic weakness.*

Should this latter affection gain the upper hand, it finally sets a sovereign veto upon further fat-production, and then thinning and marasmus may attack the *quondam* corpulent person —often, indeed, with excessive rapidity. All these conditions may be best and most instructively studied in the corpulence of sucklings, in whom the two principal types of the disease very frequently occur not only comparatively pure, but also very often (see p. 631) under the influence of accidental circumstances, of which the mode of action is known or may be determined *a priori*.

The plethoric corpulence of infants at the breast develops itself on the basis of hereditary predisposition, or without this, usually when stoutly built children receive unusually rich food, from the breast of the mother or a good wet-nurse, or still more frequently when their alimentation consists of well-mixed, but very much concentrated substitutes for milk given in too great profusion (see p. 633). If the appetite remains keen in such cases, and the digestion *intact*, which frequently, though not always, happens, the result is not merely a too great deposition of organized and unorganized tissue-material, but also an abnormally rich fat-production—*the children are crammed!* In this crammed condition they usually have a healthy, blooming color in their faces, while the development of bones, teeth, etc., takes place in them in an almost normal manner, the occurrence of rickets being at all events anything but the rule with them. In short, this form of corpulence is on the whole rather a mere excess of the physiological embonpoint of this period of life, and as such is of no very particular pathological importance. We must not, however, imagine that such crammed children are free from any inconvenience, or feel quite so comfortable as normal children who are less fat. The existing conditions are, at all events, slight lesions of health, which are due to previous deviations of a slight character from the normal state of the bodily functions (see farther on), and so far not distinctly characteristic of the plethoric corpulence of young children, since they may be observed in exactly the same manner in the anæmic form of the disease and in the corpulence of adults.

The anæmic corpulence of sucklings is, like anæmic corpulence in general, more frequently than the plethoric form the product of hereditary transmission, and is more frequently observed in boys than in girls (J. F. Meckel, l. c.). External conditions have, however, a very decided influence upon its origin and development. Among these the artificial feeding of children with improper substitutes for milk, and especially those in the composition of which the percentage of hydrocarbons and fats exceeds that of the albuminates and organic salts, holds the chief place. To this we may add deficiency in the use of fresh air, in consequence of confinement to the house in cold seasons. If now the digestion remains unimpaired by the above-mentioned method of rearing, and if further the improper substitute for milk be given in excessive quantity, *anæmic corpulence is induced;* that is to say, the deposition of fat begins more and more to prevail over *hæmatopoiesis*, the deposition of muscular flesh and bone, etc. Such children seem indeed well-nourished, but not, like crammed children, healthy in other respects. They are much paler; their lips and the visible portions of their mucous membrane have not that lively red which the corresponding parts in normally developed children exhibit; their muscles are but ill-grown, their bony frame is weak; teething occurs late and sluggishly; and finally, in the farther progress of the corpulence, signs of rickets show themselves. It is besides very common, when the above-mentioned etiological conditions of anæmic corpulence persist, that after a while lesions of digestion, partly in the form of atonic weakness, partly even in that of true dyspepsia, join company, and in the end undermine the nutritive process to such an extent that a further deposition of fat becomes impossible. Then these children, at first unnaturally fat, often collapse with extreme suddenness, and only the flabby skin which clothes the thin muscles and miserable skeleton like a loose and wrinkled bag, remains, after the occurrence of this secondary marasmus, as a memento of their former pasty condition.

Finally, *all cases of corpulence are in general more or less* a collection of symptoms of perversion of function or nutrition in various organs and apparatuses, with certain lesions of general health to which, in discussing here the general features of corpulence, we must briefly allude.

The cutaneous glands of corpulent patients, almost without exception, exhibit a tendency to very abundant secretion; and this holds good of the sebaceous follicles as well as the sweat-glands. The sebaceous secretion of the skin is, as a rule, of normal consistence, but is poured over the external surface of the body in immense quantities as liquid fat, and there produces an abnormally smooth and often distinctly shining appearance, as well as an oily and slippery quality. The tendency of the corpulent to sweating is, moreover, well-known. This peculiarity, which occurs in exactly the same manner, whether the corpulence be plethoric or anæmic, of adults or of children, is undoubtedly one of the most troublesome symptoms of the disease.

Corpulent children, like adults, besides this, very frequently suffer from *intertrigo* and *eczematous eruptions*, which usually establish themselves at the bottom of the furrows in the skin, in the covered-in and ill-ventilated portions of the body (under the breasts, in the neighborhood of the umbilicus, between the nates, as the so-called "Wolf," and in the bends of the thighs), ana thus, through their fierce itching and burning, as well as the smell of the secretion produced, which rapidly becomes fetid, certainly do not belong to the enjoyable accompaniments of corpulence. It is further well known that corpulent patients are but little disposed to make use of their voluntary muscles. This psychical proclivity to physical sluggishness frequently furnishes, indeed, a very effectual auxiliary to corpulence; but, on the other hand, it scarcely less frequently appears as an indirect consequence of this, and imprints upon the carriage as well as the movements of most corpulent individuals a peculiar character of sluggishness, difficulty, and want of energy. To this discomfort in vigorous bodily motion, or even, in some cases, actual incapacity for it (see "Special Symptomatology"), there usually at length corresponds a phlegmatic ground tone of the temperament, and particularly a prejudice against far-reaching plans, undertakings, and works of all kinds. This, when it did not originally exist in the affected person, acting as a predisposing cause to his corpulence (see above, p.), very frequently follows in its wake and may transform a personality previously brisk and intellectually active in a very remarkable manner. The respiration of the corpulent is generally, even when they are at rest, rather more frequent than that of thinner persons; and in addition, as a rule, depends less upon the assistance of the diaphragm, thus acquiring something of a costal type. With bodily movement, moreover, the *besoin de respirer* increases with extraordinary rapidity, even to true panting for air and to galloping, though superficial, respiration.

When, therefore, the patient is once forced against his will and custom to walk quickly, or in any way to bring his muscles into rapid action, he finds this usually impossible without halting after each brief advance, or interrupting his other muscular work to snatch a breath of air hastily and painfully, with widely dilated nostrils and open mouth. At the same time the patient in such circumstances almost always suffers from severe *palpitation* of the heart, which, as is usual, is connected with a troublesome feeling of oppression in the cardiac region. When at rest, on the contrary, no such abnormal sensation is usually present, while the heart's action exhibits objectively a regular, unintermittent pulsation, which, indeed, in particular cases, makes a permanent difference from the other clinical type we have before described (see p. 653). With reference to this latter, it must besides be remarked that although the above-described symptoms connected with the voluntary muscles and the respiratory and circulatory apparatus usually occur in plethoric as well as in anæmic corpulence, they are generally better marked in the latter, thrusting themselves into the foreground of the morbid phenomena which make up the disease in a sterner and more threatening manner. In connection with the anæmic habit, the deficient nutrition of the muscles, the habitual weakness of the heart's action and tendency to fainting, and finally the predisposition to atonic weakness of digestion and dyspepsia (see above), and the greater tendency to dyspnœa and cardiac attacks in anæmic corpulence presuppose a much graver affection than the plethoric, and cause the prognosis to be somewhat different in the two forms of the disease (see "Duration, Terminations, and Prognosis").

The liver of corpulent individuals in many cases on physical examination appears enlarged, in others thrust strongly upward and backward into the concavity of the diaphragm, and then its size is less easily to be estimated. If we have to determine an enlargement of the liver, the resistance of the organ, so far as it is discoverable by palpation, is not essentially changed, and it is particularly difficult to define its inferior margin through the abdominal wall.

Very frequently the existence of an enlargement of the liver is connected with a feeling on the patient's part of pressure and fullness in the right *hypochondrium*, which usually is especially severe after a full meal, and which causes the patient much torment. The *urine* of corpulent persons exhibits no constant peculiarities. Pretty frequently there is a tendency to the deposit of uric acid perceptible, less frequently to that of a large quantity of oxalate of lime. As to the condition of the *sexual function*, the most important points have been mentioned already in the Etiology. It may here be added that when the disease occurs in young adults of the female sex, the menstruation is generally scanty and often ceases before the proper time, and that fat men, on an average, have a less keen sexual appetite than thin ones. *The bodily temperature* of corpulent individuals, under ordinary external circumstances, shows no deviation from the normal degree, yet direct experiment proves that it is much more difficult to lower the temperature of a corpulent than of a thin person through the influence of cold on the external surface of the body (Liebermeister). In the same way the temperature of the internal parts rises under the influence of bodily movements, higher temperature of the surrounding medium, etc., much more and more quickly in fat people than is the case under opposite conditions of bodily habit in thin people. (As to the conditions of temperature in the corpulent in febrile diseases, see "Complications and Sequelæ.")

Anatomical Changes.

As death almost always occurs in corpulent individuals when they chance to die in a condition of corpulence, not from corpulence *per se*, but in consequence of some intercurrent affection, the post-mortem appearances, as may be imagined, are, according to the nature of this latter, very different.

We describe in the following paragraphs the anatomical changes which present themselves in the post-mortem examination of the bodies of corpulent patients, so far as these are related to corpulence as such—such modifications as are produced by the period of life and the type of the disease which is present (see above), and such accessory organic conditions as are intimately connected with the corpulence, and therefore occur with some regularity.

The bodies exhibit that abnormal external configuration more particularly described in the general description of the disease. The difference of color described as existing during life between the anæmic and plethoric skin is naturally much diminished by the corpse-like paleness of death, yet, spite of this, is still preserved to a certain and perceptible extent. The face of the corpse when plethora has existed is, as a rule, cyanosed, the hypostatic congestion of the skin being well-marked; while in anæmic cases the face is pale, and the hypostatic congestion but slightly perceptible. If, finally, we have to deal with the *cadaver* of an elderly corpulent individual, we find that those ordinary changes of outward habit which result from age, and the *arcus senilis* in the upper margin of the cornea, are usually prematurely developed and expressed with abnormal distinctness.

On section of the skin of the chest and abdomen, the thickness of the subcutaneous fat-layer on the anterior wall of the abdomen reveals itself in the most unmistakable manner, on separating it from the ribs and the muscles of the thorax, as does that of the *panniculus adiposus* of the anterior surface of the thorax, especially behind the mammæ. Direct volumetric estimates permit us at the same time to determine the amount of fat-infiltration in this portion of the subcutaneous connective tissue more accurately. The thickness of the fat-layer in the the retro-mammary connective tissue, in well-marked cases of corpulence in adults not unfrequently exceeds an inch, reaching two inches or even more; while on the anterior wall of the abdomen a padding of fat of even six inches in diameter has been anatomically observed in some cases (Virchow[1]). At the same time, after opening the abdominal cavity, the enormously voluminous and heavy great omentum, which hangs down almost into the cavity of the pelvis from the vast amount of fat developed in it, is very remarkable. Similarly upon raising the *sternum* we generally find the *mediastinal tissue* densely infiltrated with fat, and changed into a thick, broad flabby mass of it. In all these places, as well as in those we shall have to mention presently, the contents of the fat-cells of the *cadaver*, which are now congealed and no longer, as in life, fluid, are of yellowish-white color and opaque, and on microscopic examination reveal themselves as a quantity of small fat-crystals, among which there are frequently a few longer needle-crystals. These congealed contents, moreover, frequently induce a post-mortem change in form of the fat-cells; for they have frequently lost their globular form, appearing flattened against one another, irregularly indented or of regular polyhedric form. The consistency of the fat, finally, exhibits certain individual peculiarities which have been ascribed by some authors to special etiological influences.

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[1] Handbuch der Spec. Pathologie. Vol. I. (1854), p. 345.

The fat of young brandy-drinkers is said to be characterized by an unusual tallow-like hardness, and in this deviation from its usual character to approach many animal fats (the fats of wethers) (Rokitansky[1]).

The diaphragm usually appears to be thrust upwards by the pressure of the fat-layers of the abdomen; the lungs present no constant changes, and their blood-contents vary according to the blood-contents of the entire body, and the special circumstances which produced death. On opening the pericardium the heart is found externally covered with a sheath of fat, which is sometimes so vast that it covers the organ everywhere in a thick layer. This fatty growth proceeds from the sub-pericardial connective tissue, in which even under normal conditions there usually occur depositions of fat in particular localities. These are, as we know, the coronary and circular *sulci*, the lower margin of the right ventricle, the apex of the heart, and the point of origin of the great vessels. In these localities, even in corpulent persons, we find post-mortem the thickest layers of fat, but from them the fatty growths surrounding the heart spread out in all directions, and may, as we have observed, become united into one whole. Usually, however, the fat appears heaped over the right ventricle in greatest quantities and most thickly, so that this is not unfrequently entirely overgrown, while parts of the surface of the left are still free. But this enormous deposit of fat may be traced not merely above and superficially, but also extending quite deeply. In the higher degrees of corpulence the fatty infiltration proceeds from the sub-pericardial connective tissue to the inter-muscular tissue of the heart itself, of which the corpuscles of the connective tissue are increased in size by taking up fat, and appear to be metamorphosed into densely filled fat-cells. This condition of fatty intergrowth through the flesh-substance of the heart may even be recognized with the naked eye, as stripes and processes of yellowish fatty tissue may on section be seen running from the surface right into the muscular tissue which they have thrust asunder and evidently even diminished, in which case a more or less extensive portion of the flesh of the heart is evidently replaced by fatty tissue. Where, moreover, this fatty intergrowth has reached a higher pitch, we frequently find the still preserved fibre-bundles which are surrounded by fatty tissue evidently atrophic (diminished), or in a state of fatty degeneration (the primitive bundles filled with drops of fat, their transverse striping ill marked, and the attacked layers yellowish in color). It is also clear that these changes, taken altogether, must during life have not only considerably diminished the heart's working power, but also the power of resistance of its walls. In addition we may mention that those grave alterations just described are much more frequent in the corpulence of old than of young persons, children, and sucklings. In these latter the simple growth of fat around the heart is usually less extensive, the abnormal fat-deposition being usually confined to the external parts of the body. From this fatty growth around it, the heart naturally appears larger in corpulent individuals than is really the case when the circumference of the muscular structure is measured. The dimensions of the heart itself also, as might have been expected from the *data* of physical investigation during life, vary considerably in the different forms of corpulence—the organ on post-mortem examination sometimes proving to be enlarged by hypertrophy or dilatation, sometimes of normal size. In the first case the sheath (*Decke*) of the muscular layer itself may have been exposed to very important fluctuations.

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[1] Handbuch der Path. Anatomie. Vol. I. p. 284. Wien, 1846.

In the *arterial vascular apparatus* in elderly, corpulent persons the signs of chronic endarteritis are found with great regularity: dulling, thickening, and loosening of the internal coat, partial fattiness, which sometimes extends to the middle coat, depositions of chalk, etc., and, in addition, those coarser changes in form, length, and elasticity which the vessels undergo in this morbid process. In younger individuals with the anæmic type of corpulence the anatomical changes in the arteries are confined to that described in connection with anæmia—simple fatty degeneration of the middle and internal coats. This, however, is altogether absent at this age.

On the side of the venous system we may mention the occurrence of varices in the lower part of the thigh, clusters of hemorrhoids in the *rectum*, and (in men) varicoceles. These are frequently encountered in post-mortem examination of corpulent individuals of advanced age, when the disease partakes more of the plethoric character.

In this case *the quantity of blood* also in all parts, especially the size of the coagula to be found in the heart and great vessels, appears very considerable—the blood being, moreover, dark in color, dense, and solidly coagulated. In those cases, on the contrary, which during life are of the anæmic type, the internal parts are generally deficient in blood, the great vessels and heart being filled with but a small quantity of pale, loosely coagulated blood.

Macroscopic examinations of the blood of corpulent individuals during life have sometimes revealed a milky opacity of the serum (*Lipæmia*). This, which occurs most frequently in the corpulence of drunkards (Becquerel and Rodier), is otherwise no constant symptom of corpulence. More definite chemical experiments upon the blood in corpulence are altogether wanting.

Amongst the changes occurring in the abdominal region, the abnormal deposition of fat in the great *omentum* has already been recorded. On raising this, similar though less voluminous collections of fat are visible in the mesentery, and especially in the visceral folds of the *peritoneum* (for instance, in the *transverse mesocolon*, *the appendices epiploicæ of the great intestine*, *the lesser omentum*, etc.). In addition, the fatty capsule of the kidneys, which as we know is, under ordinary circumstances, a favorite locality for animal fat, is in the corpulent almost always developed into a huge mass of fat, often several inches thick, and similarly yellowish-white in color. In the midst of this, like the kernel of a stone-fruit concealed in the soft pulp, the kidney itself only comes to light on cutting through this opaque covering. Among the organs in the abdominal cavity the liver is in the corpulent above all pretty regularly the seat of anatomical changes, and exhibits the characters of the so-called *simple fatty* *liver.* From its position it is frequently to some extent thrust back into the cavity of the abdomen and rotated upward (so that during life it is often more difficult to arrive at evidence of its enlargement by percussion). Its true dimensions are, however, even when on this account an increase in its volume cannot be clearly ascertained by means of palpation and percussion, almost always considerably greater than those of a normal liver.

The consistence of such a liver is, on the other hand, not more solid—rather less so, indeed, and often soft and doughy; and in consequence of its diminished resistance, the organ, therefore, often appears flattened by the pressure of the parts which cover it in, while its length and width are increased.

The upper surface of the liver, according to the amount of its fat-infiltration, assumes a different ground-tint, sometimes more of a reddish yellow, sometimes of a yellowish brown, upon which numerous small reddish points (the central regions of the liver-islets) are usually thrown up more or less distinctly. On section, the color of the organ is similarly variegated, and when macerated is yellowish brown sprinkled with red; and on more careful examination it is manifest that the redder spots correspond more to the centre, and the yellow to the periphery of the liver-islets. The blood contents of the fat-infiltrated liver are, as a rule, diminished; the fat contents may, on the contrary, be enormously increased, so that half or even three-fourths of the entire liver surface may prove to be fat (Vauquelin, Frerichs). The liver fat varies from a fluid or semi-fluid to a firmer consistency—a peculiar form of hardness which leaves the knife-blade covered with a tallowy coating on its withdrawal after a section. This, like the analogous quality of the external fat (see above), seems to occur especially in the case of young brandy-drinkers (Rokitansky, l. c.).

The chemical composition of the fat stored up in the liver, like that of the fat of the rest of the body, is a mixture of tripalmitin, triolein, and tristearin.

On microscopic examination of sections of the fatty liver of corpulent patients, the fat-infiltration appears especially well-marked in the yellowish brown peripheral zones of the liver-islets. The liver-cells are here evidently enlarged, the corners of their polyhedral contour rounded off. The contour of the fat cells is, however, perfectly well preserved and distinctly visible, with proper adjustment under the microscope; and when the fat infiltration is but moderate, the fat in the interior of the cells is found in the form of small drops, in the presence of which the simple and complex nucleus of the cell remains distinctly visible. In greater degrees of fat-infarction these drops become confluent and form large drops, besides which smaller drops may appear; or finally the whole cell is filled with a single huge fat drop, while the nucleus has become invisible—though it has by no means succumbed—leaving no trace behind it.

The characteristics here described sufficiently differentiate the fatty infiltrated from the fatty degenerated liver. In the latter, even in the stage of the production of the finest fat-drops, the nuclei of the cells disappear and the sharp contour of the degenerated cells begins to be obliterated (Liebermeister[1]).

Of other organic changes, we may mention the occasional occurrence of *fat-infiltration of the renal epithelium* (Wagner) and *fatty metamorphosis of the pancreas* (Rokitansky), and finally we may glance at the condition of the voluntary muscles. In the higher grades of corpulence the interstitial tissue of the muscles appears to be, to a greater or less extent, infiltrated with fat, and the intervening muscular tissue atrophied. In other cases fat is found in drops arranged in rows in the primitive muscular fasciculi also, and the horizontal striping has become less clear. In short, there are here exhibited similar changes to those which are found, in a more clearly-expressed manner, in the muscular substance of the heart. It is further not improbable that, even when no fat is perceptible either to the naked eye or under the microscope, either in the muscular or other tissues, chemical examination would shew that the quantity of fat contained in them is greater than it is under physiological conditions. As to this circumstance, we have almost no positive observations, yet we have at least a few made by Valentiner,[2] in which the ethereal extract of microscopically normal breast-muscle (from the middle of the pectoralis major) of three corpulent drunkards was quantitively compared with that of three marasmic individuals. While the extract in the first case gave a percentage of 3.9 to 4.6, in the latter it gave but 1.3 to 1.7, which may very properly be regarded as an evidence of increased fat contents of the muscular system of the drunkards.

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[1] Beitrag zur path. Anatomie und Klinik der Leberkrankheit. Tübingen, 1864. p. 173.

[2] Archiv für wissenschaftliche Heilkunde. Vol. V. p. 63. 1860.

Special Symptomatology.

Analysis of the General Phenomena of the Disease, and the Post-mortem Appearances.

The functional symptoms and anatomical tissue-changes in corpulence are related on one side to the constitution and general habit of corpulent individuals, on the other to particular organs and apparatuses. We can therefore speak of the general and local phenomena in this disease.

a. *General Phenomena.*

The excessive increase in quantity of the external and internal fat of the body constitutes the characteristic and pathognomonic symptom of corpulence.

Of the manner in which this abnormal accretion of fat manifests itself histologically, and to the pathological processes to which the increase in volume of the fat-carrying layers is to be attributed, it was necessary to speak at greater detail in the introduction to this chapter (p. 628). We therefore now only briefly recall to the reader's mind that this abnormal accretion of fat in the corpulent comes to pass as well through denser infiltration of the fat tissue already existing, as through the origin and subsequent infiltration of new tissue. It is therefore a complete process. We have likewise mentioned already that the reason why the normal as well as the pathologically excessive fat deposition occurs particularly in a certain kind of tissue—the loose connective tissue (Flemming) or the fat tissue (Toldt)—is to be discovered in the peculiarly intimate relation of this tissue to the vascular apparatus, as well as its exceptional construction, which makes it seem specially adapted for fat-infiltration. These peculiarities make it finally clear why the fat deposit in corpulence is universal, but not equally distributed, and further why the fat-deposit in corpulent individuals is more voluminous where the greatest quantity of the loose tissue exists already formed, and wherever in well-nourished, healthy individuals the greatest quantity of fat is found stored up. Now, from the fact that in the higher grades of corpulence this fat-infiltration occurs in tissues which under physiological conditions contain no fat microscopically visible, we may conclude that under abnormally favorable conditions, such as the presence of abnormal quantities of fat or lipogenous material in the blood, other cells of the animal body may take up fat or produce it, and may be transformed into fat-cells, although the natural capacity for this is either smaller than that of certain cells of the connective tissue (the fat-cells *κατ᾽ ἔξοχην*), or an opportunity for this action is commonly not afforded them in like measure. Finally, as to the reason why, among cells in general, those of the liver most regularly become fat-containing in corpulence, and why a fatty liver is so frequently found in the post-mortem examination of the corpulent, we may remark that besides the general conditions which favor fat-deposition and make it possible in other regions of the body, the exceptional position in which the cells of the liver are placed as regards the stream of fat flowing into the body with the stream of nutriment, must be taken into account.

We may here once more remind the reader of the fact already touched upon (p. 615), that some time after each full meal fat is found in the liver-cells as a transitory phenomenon, even in healthy persons; and that when the diet is rich in fat, as for example when it consists of milk, there is perceptible quite a distention of the liver-cells with fine drops of fat, which, notwithstanding, under normal conditions disappears after a few hours (Koelliker, Virchow). But when the liver-cells cannot succeed in getting rid of their fat-contents within a proper time, a constant infiltration of this kind must generally occur; and it is clear that the persistence of this anomaly is threatened when

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the blood flowing through the liver is abnormally rich in fat, and when at the same time with every meal still further quantities of fat are taken up into the portal circulation.

While the abnormal fat-infiltration of some or all the tissues furnishes the ordinary characteristic of cases of corpulence in general, the *constitutional* habit of patients, as we have already mentioned in the general description of the disease, varies not inconsiderably in particular cases. If we now inquire into the deeper conditions which determine those differences, so important chemically, which manifest themselves in the form of *plethoric* and *anæmic* corpulence, our attention is specially directed to the different etiology of particular cases, and the different mode of working of the causes in action in each instance. As we have shown in the section on Pathogeny, the tendency to abnormal fat-deposition—if we pass over the possible cellular predisposition of that tissue within which the deposition of fat especially occurs—depends chiefly upon a certain complex general condition of the organism, of which the individual factors are:

1. Comparative deficiency in the oxygenation of the blood.
2. Relatively considerable quantities of lipogenous material in the blood.
3. Relatively deficient trophic and plastic energy of the tissues of the body.

One or other of these primordial changes of the somatic organization, which are for the most part (though not entirely) independent of each other, may evidently, through the influence of existing or predisposing or determining forces, be primarily produced, and thus the impulse to an unusually copious fat-production be given. Each of these causes, then, may give rise to a more or less clearly expressed degree of corpulence, while the behavior of the other two equally important factors in the production of corpulence may possibly leave plenty of room for other differences in the type of the constitution and habit in individual cases. It may easily be understood, without much discussion, that the better able the predisposing and determining causes are in any individual case *primarily to reduce the quantity of oxygen in the blood through diminution of the hæmoglobin*, the more clearly will the type of anæmic corpulence be produced. For this reason congenital hypoplasia of the blood-tissue, the female sex, advanced age, acquired flaccidity of constitution, and probably also deficient sexual function, predispose to anæmic corpulence. This is, moreover, under certain circumstances, provoked by improper, insufficiently hæmatogenous diet, bodily inactivity, and morbid processes, which specially beget oligocythæmia. On the other hand, *a primary increase of lipogenous materials in the blood* leads to increase in the volume of the blood left, hypertrophy, and *plethoric corpulence.* It is no matter whether this superfluity is produced by increased reception or diminished decomposition of the material, so long as it is sufficiently large and lasts a considerable time. For this reason plethoric corpulence arises, in the general form already described, most easily under the determining influence of a voluptuous mode of life, intemperance in the pleasures of the table, and the abuse of alcohol ; and it is more frequent in men than in women, because the former are fonder of exposing themselves to these injurious influences. Where the excess of lipogenous material, and especially the albumen of the pabulum, is very great, and when the composition of the blood, as well as the outer and inner conditions of the individual existence, favor the simultaneous accretion of organized albumen and the formation of red blood-corpuscles, the health may be otherwise almost undisturbed, the corpulence appearing more as a simple excess of physiological embonpoint, and as a complete pendant to the fattened condition of the domestic mammalia. It then has the character rather of an anatomical curiosity than of a real disease. It, however, not unfrequently conceals within it the germ of other lesions (see "Sequelæ"), and is only to be regarded with indifference when no severe diseases of another kind are threatening (see "Prognosis"). On the contrary, when, with a great stock of lipogenous material, the conditions are unfavorable to blood-formation and the accretion of organized albumen, hybrid forms of corpulence are produced, in which the fullness of the vascular system contrasts with paleness of complexion and badly nourished muscles—forms which present in their external character a peculiar mixture of want and superfluity, of strength and weakness, and which are therefore harder to classify. Since, further, partly from advancing age, partly from external conditions (especially deficient bodily exercise), and partly from intercurrent diseases, the danger of a subsequent hypoplasia of the blood is imminent even in plethoric corpulence, it follows that most cases of this kind, as they advance, lose their original type and gradually assume a hybrid, and finally, even anæmic character. It also follows that, however great, in many respects, the difference of the first approach of corpulence may seem in different cases, they all tend towards the anæmic type, even when they did not belong to this originally.

b. *Local Symptoms.*

In the *external skin the increased secretion of the sebaceous follicles* (*seborrhœa*) *and of the sweat-glands* (*hyperidrosis*), is specially worth mention. The seborrhœa of corpulent individuals must be considered as analogous to the deposition of fat in other tissues, but with this difference, that here it occurs in a deciduous tissue (the epithelium of the sebaceous glands) which, a prey to perpetual destruction, has to furnish the secretion of this cutaneous gland. With great infiltration of fat the destruction of these deciduous cells will therefore be more rapid, and the fatty secretion produced by them must escape in greater quantities than is usual under ordinary circumstances. The *hyperidrosis* of the corpulent is a commonly recognized phenomenon, but one of which the causes are but little appreciated. To understand the genesis of this symptom a little better, it is not necessary to go into any wide discussion concerning the physiological process of the secretion of the sweat, and the share which blood-pressure, the nervous system, and the secretory parenchyma of the glands themselves may each separately take in it. For our practical object it is here enough simply to understand what physiological significance this secretion has for the organism in general, and what internal, as related to external conditions, are found by experience to produce profuse sweating. The sweat secretion has evidently, as its physiological end, *the production of a cooling of the entire body* by irrigating its surface with a watery, easily evaporating fluid, as soon as *there* *is a danger of a rise of its temperature above the normal level*, either through *increased production* or *diminished abstraction of heat.*

Now, the corpulent are, even when at rest, much more than those of normal build or thin persons, exposed to a danger of a rise of their bodily heat from higher (atmospheric) temperature, deficient ventilation, and excessive humidity of the air; since their thick padding of fat affords them a very effectual protection against the cooling of their internal parts, and their corporeal superficies is small as compared with their mass;[1] and therefore the amount of heat given off to the surrounding medium by conduction, radiation, and evaporation will be relatively small. Upon the presumption, then, that the sweat-gland apparatus works in the corpulent under the same laws as regulate it in the healthy, the former ought to sweat more easily and more frequently in all circumstances than the latter—a conclusion which is confirmed by daily experience, and therefore may serve to support the foregoing presumption. Another reason also which is important, as accounting for the hyperidrosis of the corpulent when in bodily action, is to be found in the great mass of their bodies. To put them in motion and keep them moving demands a much greater expenditure of voluntary muscular force than is the case with the smaller mass of healthy or thin persons. But as the muscle which does more mechanical work than another *produces also more heat* (Heidenheim), it must be accepted as a fact that not only is less heat given off by the corpulent, but that when in motion they produce more heat, and that the danger of overheating of the internal parts of their bodies is infinitely greater. Now, the secretion of sweat, as a regulatory function of the general organism, works against this unfortunate condition in this manner, that in the corpulent it takes place as a consequence of the performance of mechanical work, not only with extraordinary rapidity, but with excessive profuseness; so that whenever they stir themselves up to violent motion they immediately appear bathed in perspiration.

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[1] As we know, the globe of all geometric forms has the *greatest solid content with the smallest circumference.* The nearer, therefore, the human body approaches a globular form the smaller relatively will be its surface.

When, therefore, Shakespeare makes Sir John Falstaff say, when involuntarily placed in this position, that he feels as hot "as molten lead," and complain of the "tons of sweat" he has poured out, these outbursts of comic despair are, it is true, hyperbolical, but certainly also most significant as to the actual condition of such patients. We are then, as has been shown, in a position to refer the interesting phenomenon of hyperidrosis in corpulence to the very laws which the physiological secretion of sweat follows; and this pathological phenomenon appears in the general symptomatology of the disease only as the excess of a normal action, the conditions having become unusually favorable for the physiological process, and the secretory apparatus working according to the ordinary rule. A further frequent consequence of the increased skin-secretion, and the collection of the secreted sebum and sweat in the covered portion of the sulcated surface of the body, where this is not sufficiently cared for, is the decomposition of these secretions, which occurs very easily, and the development of rancid and putrid products, which are not only very ill-smelling, but also, from their acridity, irritate the skin and give rise to intertrigo, eczematous eruptions, etc. Another cause of the appearance of the skin-diseases from which so many corpulent persons are liable to suffer much is the mechanical irritation of the chafing to which the skin of these folds is exposed during bodily movement, and which may be much increased by the pressure of tight articles of clothing—stockings, etc. The symptoms connected with the external skin form, then, a whole of which we may easily obtain a synopsis, their logical connection with the original disease being grasped without difficulty.

This, however, may be affirmed of most of the remaining symptoms of corpulence, and first for the phenomena of the voluntary muscular apparatus. The difficulty of bodily motion is, like the slight weariness of the patient from increasing his pace, raising weights, etc., the immediate consequence of the great weight of the body—the heavier burden which has to be lifted, urged forwards, and kept in action. There results further, from the patient's experience of this aptitude for being soon tired, a mental distaste, which causes him even in anticipation to be shy of much movement, and very easily leads to habitual corporeal sluggishness, where the disease did not originally proceed from this. That very troublesome feeling of heat and tendency to sweating, and, last, but not least, the tendency to dyspnœa and cardiac palpitation which quickly follows upon bodily motion, are great stumbling-blocks in the exercise of the patient's voluntary impulses, and often imprint on his whole personality a stamp of prudence and circumspectness; so that courageous boldness and bold venturesomeness seem to him hazardous and improper, even in cases where the end is attainable without much *bodily* action, and simply through vigorous *mental endeavor.*

The rapid, though shallow respiration to which the corpulent are subject even when at rest, results principally from the hinderance given to the actions of the diaphragm, which, by the pressure of the enlarged liver, and the fat-masses within the abdomen and on its anterior wall, is more firmly fixed in the expiratory position than is the case in thin persons. This is also the reason of the increased functional activity of the superior respiratory muscles (intercostals, scaleni), and produces the costal type of respiration even in corpulent *males.* The *great tendency to attacks of dyspnœa* from bodily motion simply arises in no small degree from this mechanical hinderance to respiration, which makes a complete ventilation of the lungs and elimination of the stagnant carbonic acid, by deep respiratory efforts, extremely difficult; and no shallow breathing, however frequent, can fully compensate for this loss of power. On the other hand, it is also a consequence of the absolute increase of work which the heavy mass of the body imposes on the corpulent for their locomotion, and demands from their muscles, and it is therefore connected with increased production of carbonic acid. Finally, in the high grades of polysarkia, another most important force—namely, functional *insufficiency of the heart,* comes in to assist in developing these attacks of dyspnœa, and stamps them as not only a very unpleasant symptom of the disease, but one which is of immediate danger. This lowering of the motor power of the heart, which betrays itself in habitual weakness of that organ, as well as rapid fatigue of its muscles after strong contraction (see p. 658), has its ground above all in the anatomical changes more particularly described already. The simple growth of fat around the organ, to say nothing of the more important fat-infiltration of its intermuscular connective tissue, must in the long run make the maintenance of an evenly energetic action of the heart more and more difficult, and favor the occurrence of paroxysmal congestive phenomena in the pulmonary circulation, as often as, in consequence of bodily exertion, mental emotion, etc., an acute over-stimulation of the heart has taken place. The paroxysmal dyspnœa which thus originates, becomes, however, habitual, whenever the muscle of the heart has become atrophic or fattily degenerated from the pressure of the fatty tissue which weighs upon it, and has new points of origin within its very structure, and the capacity of motion for the patient is naturally diminished in all directions to a far greater degree than was the case in the earlier stages of the disease from the cause already more particularly described.

The attacks of palpitation have the same cause as the dyspnœa, and proceed, as this does, from the easily fatiguable condition of the heart, for which the greater demands made upon it and its absolutely diminished power must bear the blame. Finally, it is easily intelligible without minute analysis, why all the phenomena in connection with the voluntary muscles and respiratory and circulatory apparatus just described, occur much earlier, more intensely, and more threateningly, in the anæmic form of corpulence. Here, however, the primarily existing oligocythemia, with its necessary consequence—the deficient oxygenation of the blood, contributes a very aggravating factor, which makes itself from the commencement felt as a destructive force upon the functional restitution of the working muscular system of both body and heart, as well as the excretion of carbonic acid from the respiratory surface of the lungs.

The frequent *occurrence of uric acid and oxalic acid* sediments in the renal secretion of corpulent individuals is probably less a direct consequence of the corpulence than a co-ordinated phenomenon which is due to similar causes. For, while a false relation between the quantity of the nutrient material of the blood and the amount of its oxidization, together with a sufficiently large assimilation of food, is the primary condition of a great deposition of fat, this evidently also acts as a predisposing cause of the development of a great number of azotized and non-azotized compounds, which, in contradistinction to the proper ultimate compounds (urea, carbonic acid), must be looked upon chemically as a product of imperfect oxidation. Just as corpulent persons then, and persons with a tendency to become so on a rich diet, put up more fat than those who have no such tendency, they frequently seem also to excrete a greater quantity of uric acid and oxalates. For the rest, more accurate quantitive estimates respecting both the actual quantity of uric and oxalic acids, and of the relative quantity of uric acid and urea, excreted in well-marked cases of corpulence, are altogether wanting. Finally, the habitual existence of uric acid in the urine affords only some probability, but by no means certainly proves, that there is any absolute increase of uric acid production in any given case (Bartels [1]).

Complications and Sequelæ.

The corpulent show not only a *predisposition* to a number of secondary affections, but also, with regard to purely accidental morbid processes, a very different (and in general less) degree of tolerance than healthy persons. In both directions, therefore, an investigation of the complications and sequelæ is, theoretically and practically, of importance. Among the most frequent secondary processes in corpulence are *acute and chronic catarrh of the mucous membrane of the respiratory apparatus.* This catarrh very often depends on so-called "colds," to which corpulent people, with their great tendency to perspiration, are unusually disposed. It is also, however, in many cases due to the above described lesion of the heart's action; in addition to which, as a further favoring condition which brings this to light, we must add in many cases a pressure of the fat-masses of the abdomen upon the abdominal aorta, and a consecutive reflux of the blood towards the respiratory organs. The not less frequent *acute and chronic catarrh of the digestive apparatus* has its root to a great extent in the common lesion of circulation commencing in the heart; and also perhaps in that hinderance of the hepatic circulation, to which the congestion of the liver-cells consequent upon their fatty infiltration may give rise. Besides this, we may often have the luxurious mode of life to which many corpulent persons, spite of their increasing growth in circumference, remain weakly addicted—the overloading the stomach with a quantity of all sorts of food, often difficult of digestion, with tidbits, etc., the misuse of alcoholic drinks, etc., all tending in time to make the intestinal tract very liable to disease, or at least to intercurrent affections. If these dyspeptic processes go on long enough, they will naturally undermine, by the process of inanition which they promote, the basis of the corpulence itself, and then, even in the case of plethoric corpulence, emaciation, and finally marasmus, begin with a change for the worse in the complexion, pallor of the whole surface, etc. A further frequent complication of corpulence are those varicosities of the rectum—the so-called hemorrhoids, which are commonly represented as one of the phenomena of the general abdominal plethora and as a special characteristic of this. The plethoric condition of the blood (the increase of the volume of the blood), as well as the special lesions of circulation existing in the abdomen, certainly play a most important rôle in the origin of that enlargement of the vessels of the abdominal plexus, and their frequent occurrence in corpulence, therefore, appears in many cases the direct consequence of this latter disease.

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[1] Deutsches Archiv f. klinische Medicin. Vol. I. p. 13.

On the other hand, however, in many other cases it is just as certain that the hemorrhoidal affection has developed itself before the manifestation of the corpulence, and therefore cannot be considered as the immediate consequence of this.

We are therefore compelled further to assume that the coincidence between corpulence and hemorrhoids, in a certain and not small class of cases, has some deeper constitutional ground, which leads to a conclusion that individuals with a relaxed constitution and natural tendency to corpulence have at the same time frequently a deficiency in the constitution of their venous-vessel walls, and with this a tendency to varicosity. These vascular enlargements occur sooner or later in the course of life, especially in those regions of the venous system which from their position are especially exposed to pressure, hard work, the relaxing influence of heat, etc., and therefore, especially in the hemorrhoidal plexus, the cutaneous veins of the lower extremity, the *funiculus spermaticus*, and some other places. Perhaps the predilection which the skin-disease, known as *acne rosacea*, has for the nose and face of corpulent individuals, may be considered as connected with the simultaneous constitutional predisposition to fat and varicose degeneration of the veins. This skin affection, indeed, is developed most frequently in plethoric corpulence, and here again especially in those cases in the origin of which the misuse of alcohol has played an important part. Nevertheless, we should decidedly fall into error if we definitely connected chronic inflammation of the sebaceous follicles and vascular dilatation with this, since it is surely very well known that this unpleasant coppery red coloring of the nose and face often occurs in persons who are quite temperate, such as old women (Hebra), without any known external exciting cause. We are, therefore, here compelled to recur in many cases to deeper reasons, and cannot look on this frequent complication of corpulence with *acne rosacea* simply as due to an entirely external connection between them. It may, however, in many such patients be truly ascribed to an intemperate mode of life. On the side of the *arterial* vascular apparatus the frequent simultaneous occurrence of corpulence and atheromatous degeneration of the arteries is especially worthy of notice clinically, because that plethoric condition of the blood, which is at the bottom of many cases of corpulence, in connection with the consecutive hypertrophy of the left side of the heart and abnormal fragility of the arterial vessels, produces in plethoric corpulence an extraordinary tendency to *rupture*, which may be fatal to the patient through sanguineous cerebral apoplexy. The unusual frequency of apoplectic seizures in plethoric corpulence has led physicians to describe the corpulent as the "apoplectic" habit, and to use both terms promiscuously in practice.

This method of designation involves a want of clearness only in so far as it anticipates in corpulent individuals of youthful years future dangers ; and not because apoplectic seizures are at all uncommon in the anæmic corpulence of elderly persons. *In the anæmic corpulence of advanced life ruptures of the blood-vessels of the brain occur also, and by no means exceptionally, but very frequently*, because atheroma of the vessels of the brain is by no means infrequent with them, and this vascular degeneration is of all etiological influences the preponderating cause of the rupture of arteries. Hence, the tendency of corpulent individuals to apoplectic seizures is chiefly due to this complication on the side of the arteries, while among the most important of the secondary causes stand plethora and hypertrophy of the heart when they exist. But as corpulence is frequently, and atheroma almost as a rule, met with in elderly persons, this disposition often appears as an attribute of that period of life in which corpulence most frequently occurs. As a further and very common accompaniment of corpulence, *rheumatic* affections of the muscles, sheaths of the tendons, ligaments and capsules of the joints, may be named—the character of these being that they are sometimes vague and sometimes fixed in one spot. We must, however, remark that the febrile disease to which the term "acute rheumatic arthritis" is strictly applied, has no perceptible predilection for fat people, and that it is only that other painful affection of the motor apparatus known by the name of "rheumatism" that is comparatively frequently met with in the corpulent. We shall not here discuss the question how far any general constitutional cause lies at the bottom of this coincidence, as a direct proof in support of such an opinion cannot at once be brought forward. The so-called "colds" to which fat persons, on account of their tendency to hyperidrosis, are exposed (see above), act at all events in many cases as an important external cause of the occurrence of rheumatic attacks in the corpulent. Now, while a genetic connection between the constitutional affections which exist in corpulence and rheumatism cannot be certainly established, such a connection between the corpulent constitution and gout can be accepted without any question. This much is empirically certain: that an unusually large number of gouty persons suffer, at the same time, from corpulence, and it is also not very difficult to deduce an inner relationship between both morbid processes. Both affections, so far as their genesis is understood, depend upon important congenital (hereditary) anomalies of the physiological chemistry (Stoffbewegung), which, moreover, in both usually first develop themselves in a most marked manner in the physiological decadence of life, and under the determining influence of a too rich diet and the abuse of spirituous liquors. In both, finally, this anomaly in physiological chemistry, or constitutional morbidity, is to be found in a sluggish oxidation of the material taken in with the diet—in a wrong relationship between the amount of oxygen and the amount of consumable material in the blood. Now, just as the increased deposition of fat and the development of corpulence result from the insufficient consumption of the *non-azotized* products of the decomposition of the circulating albumen of the pabulum, in many cases a superfluity of lithic acid in the blood simultaneously results from the imperfect oxidation of the *azotized* products of the decomposition of the circulating albumen; and this, according to Garrod,[1] is the primary condition of gout. In the development of an attack of true gout, we must then have a temporary retention of this lithic acid in the blood, or a retarded excretion of it through the kidneys. In short, there must be additional conditions, so that by no means all corpulent individuals with a habitual lithic acid diathesis suffer from veritable gout. The relation of polysarkia to lithiasis is to be understood in the same way as its relation to gout, the anomaly of physiological chemistry existing in corpulence involving a predisposition to *lithiasis*, inasmuch as it favors the production of great quantities of lithic and oxalic acids. Here also, in order that the stony concretions shall occur, a further particular condition of the urinary apparatus is necessary, which *may* indeed be the case when corpulence exists, but by no means *must* always be the case. Among other complications and sequelæ of corpulence, *diabetes mellitus* and *carcinoma* of internal and external organs (stomach, breast, etc.), may finally be mentioned. The special predisposition of the corpulent to *diabetes* has been particularly insisted upon by Seegen,[2] that to cancerous diseases by

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[1] The Nature and Treatment of Gout. London, 1859.

[2] Der Diabetes mellitus auf Grund zahlreicher Beobachtungen dargestellt. Leipzig, 1870. Cap. II. Conclusion.

J. F. Meckel, Wunderlich,[1] and others. We cannot here speak more particularly of the frequent development of diabetes in corpulent individuals, and refer therefore to the chapter on diabetes in this volume. The coincidence between corpulence and carcinoma is produced much more by the period of life in which both diseases are observed than through direct relationship. When a corpulent man becomes diabetic or carcinomatous, a rapid reduction of his circumference through disappearance of the huge mass of fat may be observed. It is, therefore, in all cases a very suspicious sign when corpulent patients, without corresponding therapeusis, suddenly begin to grow thin and lose their padding of fat.

The above-described complications and sequelæ of polysarkia belong especially to those cases of the affection which occur in adults. As to the complications and sequelæ of the corpulence of young children and sucklings, we have already remarked upon all that is most essential with regard to the general type of the disease. The enumeration of these secondary affections was most suitable in that place (see p. 656), because they furnish important points of distinction between the two forms of infantine corpulence (the *anæmic* as opposed to the *plethoric*), and really form a part of the description of the disease itself. Among these complications just described, we may again particularly mention catarrh of the mucous membrane of the respiratory tract as not being the exclusive property of adults, but being most frequently observed in corpulent sucklings.

Of the greatest and most practical importance is that particular behavior of the corpulent constitution with regard to intercurrent severe illnesses of every kind, which we have spoken of just now as well as in the introduction. We have now to declare that corpulence is not ascertained to insure any immunity from any disease to which thin persons are subject, and that the more severe acute febrile diseases (typhus, acute exanthemata, pneumonia, erysipelas, acute rheumatism, etc.) attack fat persons just as frequently as thin. The corpulent are therefore, as compared with the thin, by no means favorably situated as regards their morbility; while, on the other hand, it is a very serious consideration for them, *that all severe morbid processes, and especially all affections accompanied by intense fever, run their course with unusual malignity.* This idiosyncrasy, well known and appreciated by the physicians of classical antiquity, may be regarded as a fact which is raised above all doubt and fully proved by the medical observation of some thousands of years; it surely, in the highest degree, challenges general hygienic interest over the whole circle of precise medicine. In modern times, Roeser, Wunderlich (l. l. c. c.), and Liebermeister[1] have more especially occupied themselves with this circumstance, and the latter author has undertaken the honorable task of theoretically explaining these pathological facts so far as they concern febrile diseases. The most important fact is, however, that all *febrile* diseases of great intensity take on the so-called adynamic form (asthenic, putrid, pestilential), or, to express ourselves more precisely in modern style, are connected with signs of beginning and advancing paralysis of the heart much sooner in the corpulent than in thin persons, and therefore more frequently end in death. But non-febrile diseases of an exhaustive character are also worse borne by the corpulent, and likewise comparatively early take on the *adynamic* character, although the difference is not so important in the non-febrile as in the febrile diseases. The reasons of this premature adynamia of the heart, and of the unusual general prostration of corpulent persons in exhaustive diseases of every kind, are more particularly the following:

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[1] Handbuch der Pathol. und Therapie. Vol. IV. p. 548.

1. The already described *anatomical* changes in the *heart* of corpulent persons. These produce, especially in advanced corpulence, a cardiac weakness *per se*, which naturally, with the concurrence of any severe complicating disorder, must comparatively soon reach a high and *menacing* pitch.

2. The deficient *functional restoration of the muscles of the heart*, as well as *the muscles of the rest of the body.* It has been more particularly described in speaking of anæmia (see p. 381), that the muscular tissue, during continuous work, requires a

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[1] See Vol. I. of this Cyclopædia.

continual supply of oxygen, because the synthesis of unoxidized substances can only take place through the concurrence of oxygen.

Now, *in cases of anœmic corpulence in particular* (and these, as experience teaches, form the bulk of all cases), in consequence of the existing oligocythæmia, the amount of oxygen in the blood is already itself less than it should be, and therefore the possibility of functional restoration of the muscular tissue is less. If, then, through exhausting diseases, and especially of a *febrile* nature, a further lesion of the red corpuscles (an accelerated destruction or deficient new production of them) occurs as an additional injury to the heart and the other muscles, the weakening influence of this new calamity will sooner than otherwise make itself felt in a fatal manner. The heart will earlier strike work, the general debility of the patient will be greater, and the lethal catastrophe will, under the given circumstances, occur more easily.

3. *The comparative smallness of the surface in corpulent persons.* The injurious influence of this on the progress of intercurrent disorders is specially felt in febrile complications, where, however, it is felt in a double manner (Liebermeister, l. c.); the smallness of the surface of the body, in connection with the thickness of the fat-padding, hinders the giving-off of heat in fat persons in this manner, that the temperature of the internal parts (similar intensity of the febrile process being supposed) in them earlier reaches and remains at a pitch which acts injuriously upon the heart's action and the remaining vegetative functions of the body. In the corpulent, therefore, hyperpyretic temperatures occur comparatively more easily than in thin persons, and fat persons are in a much more immediate manner endangered by *febrile heat* than those who are less fat, or thin; and, therefore, febrile affections, even if *the course of the fever itself be left out of the question*, are much more frequently unfavorable in their termination than in the former.

In the second place, however, the possibility of *mitigating* the increased temperature *artificially* by direct abstraction of heat, and averting its pernicious action on the tissues by cooling applications at the right moment, is limited much more in fat people on account of the great mass of the body, with comparatively small superficies, and the thickness of the protecting layer of fat. From the great importance of the hydriatic method and the blessed rôle it plays, as we know, at the present time in the treatment of febrile affections, the difficulty which exists of *really cooling* corpulent patients by means of cold baths, packing, etc., or *the inadequacy of the hydropathic method*, gives rise to a great additional difficulty, which is expressed in the greater mortality among corpulent patients.

But, further, even in favorable cases where the exhausting disease (especially when it is febrile) is happily got over by the corpulent patient, the prejudicial influence of the abnormal bodily habit manifests itself perceptibly and clearly even during the period of convalescence. Corpulent convalescents are comparatively slow in recovering from severe illnesses, and comparatively often imperfectly recover. Their physical and mental capacity for work is recovered later, and often never regains its pristine level; and as a consequence *an increased tendency to abnormal fat-deposition remains*, with the *anæmic* form of the disease into the bargain. The probable cause of this abnormal course of convalescence is to be looked for in the *relaxed constitution* of corpulent individuals. This produces *sluggish deposition of organized albumen*, with a slower nutrient restitution of the tissue which has been used up (consumed) during the complicated illness, and, moreover, a *hypoplasia* of the tissue-elements of the blood, and with this naturally a much more obstinate and persisting oligocythæmia, with consecutive tendency to fat-production. As we see, it is therefore to a certain extent possible theoretically to account for the greater malignity of severe intercurrent affections in corpulent individuals, and the anomalies connected with their convalescence from such affections; and thus to explain a phenomenon which, as was mentioned, had rightly occupied the attention of individuals from time immemorial.

Diagnosis.

No very subtle methods of examination are necessary to make the diagnosis of corpulence in advanced cases of the disease; the corpulent patient impresses even the untutored eye of the laity, through his general external appearance, in such a manner that there can be no question about "overlooking" the disease!

But a "mistake" as to the abnormal condition ought to be, with a little attention, difficult for the physician, since there are in fact but two conditions with which corpulence could, under any circumstances, be mistaken. These are *extensive anasarca* and *extensive emphysema* of the skin, and both may be easily diagnosed from simple fat-infiltration of the panniculus by means of *palpation* and *percussion.* Palpation in dropsy gives us the well-known doughy character of the general surface, which may be recognized by the pit which remains in it after compression with the finger; in subcutaneous emphysema there are the peculiar feeling and sound of crepitation. The sound on percussion is, moreover, dull in dropsy; clearly tympanitic in the raised and bloated portions of the body in subcutaneous emphysema.

The physical characters of the external envelope in corpulence are quite different from these. There is tense, elastic resistance with muffling of the percussion sound over the thorax and abdomen on sufficiently strong percussion, but not complete dullness. It must, however, be remarked that many corpulent persons become dropsical towards the close of life (see "Terminations" in the following pages), in which case the physical signs of dropsy are combined with those of corpulence, and it is then sometimes difficult to estimate the amount of the latter on account of the presence of the former.

There is in many cases just as little difficulty in distinguishing the *type* of corpulence as there is in making a general diagnosis of the disease itself. The differential diagnosis between plethoric and anæmic corpulence is always easy when the type is clearly marked—that is to say, when, together with the cardinal symptoms of change in the external aspect of the body, the vascular injection of the surface and the color of the face and skin speak unambiguously for plethora or anæmia, and when the fullness of the pulse and the volume of the heart may be brought into harmony with one or the other abnormal condition of the blood. On the other hand, it is perhaps necessary here to mention that the color of the face *alone* is not a perfectly trustworthy point on which to form a judgment, since cases of anæmic and hybrid corpulence exist, in which a diffused redness of the face or an *acne rosacea* in the region of the nose may stimulate a plethoric condition which, notwithstanding, does not really exist. Habitual congestions of the face occur only in anæmic individuals, and *acne rosacea* develops itself, as was mentioned before, even in persons from whom every suspicion of plethora must be very remote. In short, the vivid injection of the face is not necessarily a consequence of an increase in the volume of the blood, but may also be an effect of a lesion of circulation. It is therefore advisable in doubtful cases, on the other hand, to examine into the history and etiology, *in concreto*, to ascertain the causal forces which have really been active; and, on the other hand, by means of a careful inspection of the rest of the surface of the skin and those portions of the mucous membrane which can be got at, and by means of a physical examination of the circulatory apparatus, to get as clear a glance as possible into the actual condition of the mass of the blood, and thus to form an approximate conception of its general richness in red blood-corpuscles. To form a general judgment concerning the particular nature of individual cases from the particular data thus found, is thus necessary for the physician, because, as we may remark in anticipation, the treatment of plethoric must be in many points essentially different from that of anæmic corpulence, and it is quite unpermissible to treat all corpulent persons —simply because they are all corpulent—exactly in the same stereotyped fashion.

Duration, Terminations, and Prognosis.

Corpulence is almost always a chronic, gradually originating, most frequently progressive—and usually, when once developed, persistent affection. Excepting those cases in which suitable and efficacious treatment is successful in putting a stop to a further deposition of fat, or those in which the patient, in consequence of intercurrent severe complications (such as obstinate dyspepsia, febrile processes, carcinoma, diabetes), falls into marasmus, and so naturally ceases to be corpulent, we may say that a spontaneous involution is seldom observed. An important *exception* to the rule in this last respect is, however, to be found in *the corpulence of the period of lactation.* In this form a spontaneous cure and limited duration are even as the rule observed, because, as experience teaches, if once the patients succeed in getting happily through their first year, in the second they usually gradually get rid of their superfluous padding of fat and grow thin. In this fact lies a chief proof of the justice of our opinion, most definitely expressed before, that the corpulence of the early period of life has more of an accidental character, and takes a less deep hold, not being favored by the natural process of the physiological chemistry of that earliest period of life. For, even when no deep tendency to the disease exists, the peculiar nature of the alimentation, together with the bodily rest, can produce during the period of lactation a huge padding of fat, which will afterwards undergo involution, and disappear as soon as the child, *after passing through its first year*, is more and more weaned from the breast, and on learning to walk throws its body more and more into action. Even when a not very strong individual predisposition to corpulence is congenitally present, the external conditions for the duration of the corpulent habit through the remaining years of childhood, youth and puberty, are naturally so unfavorable, that often enough, *spite of the persistence of the tendency to the disease*, this may become at the tenth year as good as latent, and first again distinctly manifest itself only in advanced age. When, on the contrary, the abnormal corpulence *lasts considerably longer than the first year*, or begins to develop itself *after the first year* in children and young persons, *in an apparently spontaneous manner*, there is usually a presumption of a very strong (congenital or acquired) predisposition from the beginning, and it must usually be concluded from observation of the facts before us, that the nature of the disease is obstinate, and its duration cannot be reckoned. Then, again, it is rather different with the duration of the disease when it occurs in youth *symptomatically*, for instance as a sequela of chlorosis, acute anæmia, etc. Here the persistence of the corpulence depends chiefly on the duration of the original disease; and where this can be got rid of, or gradually disappears of itself, a reduction of the circumference of the body and of the padding of fat is pretty frequently observed as a consequence after some time (weeks or months). The idiopathic corpulence of advanced life, finally, consists in an obstinate and protracted process, which does not in the slightest degree tend to spontaneous involution. This fact should not seem at all strange if we only consider that the anomaly of physiological chemistry, which lies at the bottom of the abnormal tendency to fat-production (see above), does not in the least diminish in the declining period of life through the natural modification of physiological nutritive processes, but, on the contrary, increases more and more. Besides, it is frequently the case that the external conditions and habits of life of the patient are calculated to give an impulse to the further accretion of fat, and continue to do so.

The *terminations* of corpulence may be complete or incomplete cure, unalleviated persistence, progressive disimprovement, and finally death. A complete and *spontaneous* recovery is, as before remarked, frequent only in the adiposity of sucklings; in all other forms it is extremely rare. A complete recovery through therapeutic rules of temperance is rather to be expected in the symptomatic forms of the disease, that is, if the original disease is itself curable — but may now and then, though not very often, occur in other cases which have not progressed very far in their development. A very high degree of corpulence, on the contrary, admits of but a very slender expectation of a natural or artificial radical cure; while even in the corpulence of sucklings we may affirm that the more pronounced the condition of corpulence, and the less disposition to resolution it shows after the course of the first year of life, the worse are the chances of total recovery. The reasons of the rarity of a radical cure in advanced cases of all kinds lie partly in the power of predisposing causes (heredity, period of life, sex, etc.), under the influence of which the disease generally occurs, and against the weight of which every form of prophylaxis and therapeutics is known from the earliest times to be much less powerful than it is against external influences—partly in the limited choice of means with which we may oppose the condition without danger to the patient (see "Therapeutics"). Besides this, it happens that the pathogeny of corpulence is, to a certain extent, though by no means fully, hidden from us; and that cases, in fact, occur, in which the disease is produced, not under the ordinary well-known circumstances, but *through some unknown inner predisposition* (see p. 628), and that the therapeusis, contending against such an invisible foe, remains itself necessarily more of a riddle than it would otherwise be.

We may, however, even with well-directed and prudent therapeutic treatment, obtain no perfect cure of the condition, but only an improvement—*an imperfect cure.* It is clear, however, on the other hand, that the prospect of a cure in any case is the greater the more external circumstances—against which the therapeusis can interpose, and of which the removal lies in the power of the physician and the patient—have provoked and maintained the corpulence. Now, since injurious influences of this kind lie more frequently at the bottom of plethoric than anæmic corpulence, and of that of men than of women, we more frequently observe, in the former than in the latter case, some decided benefit from treatment and transient improvement. We must, however, always, even when under the impression of a transient result from treatment of as favorable a nature as possible, be prepared for a *return* of the disease, which will *probably*, we may almost say certainly, take place; always supposing that we have not to do with a case belonging to one of the categories mentioned above (corpulence of sucklings, or symptomatic corpulence dependent on curable primary disease), in which a radical cure, as experience teaches, frequently takes place. But unfortunately the endeavors of the physician very frequently come to nought—in cases in which a well-grounded expectation of temporary improvement, through strict carrying out of the prescribed therapeutic treatment, may exist—through want of energy of will on the part of the patient. At other times also it may fail through adverse incidents (complications) which prevent the carrying out of the usual and efficacious curative rules of temperance. The disease, then, often remains not only uncured, but unimproved—remaining for the present a stationary complaint.

Many advanced and severe forms of corpulence, which, without a suitable and continually renewed therapeusis, would undoubtedly assume a progressive form, exhibit the stationary character. We must often in such cases be satisfied if we can prevent a disimprovement in the condition by a careful watch over the mode of life and persevering use of suitable curative agents; thus, as long as possible, conjuring away the dangers which threaten the patient from the most different sides. That under such circumstances the palliative treatment, which to the disgust of the patient demands from him renunciations and discomfort, most usually ends in shipwreck, or is rendered impossible by intercurrent events, is intelligible without further elucidation.

When left to themselves, most cases of corpulence (except those during the first year of life), as we have already said, run a *progressive* course, during which the inconveniences of the patient increase at the same time with the circumference of the body, until at last, earlier or later, death entering puts an end to the increase of the corpulent tendency. This *lethal termination* may be brought about by *excessive corpulence itself*, as well as by *complications*, *consecutive conditions*, and *incidental intercurrent diseases*, and takes place in different ways in different cases. Corpulence becomes fatal, *per se*, more especially when a great growth of fat takes place around and in the substance of the heart, with atrophy and degeneration of its muscular substance, as one of the phenomena of an advanced condition of general fat-infiltration, developed during the course of the disease, and when, in consequence of these anatomical changes, the circulation suffers distress. In such cases death may often occur pretty *suddenly* from *syncope*, and, indeed, particularly easily after violent efforts, mental emotions, etc., and the examination of the body then often reveals no other point on which to rest an explanation of the unexpected lethal catastrophe. The patients more frequently die with *dropsical symptoms*, which gradually supervene, get the upper hand more and more, and finally, in the form of cerebral and pulmonary œdema, put an end to life. That an oligocythæmic form of constitution gives a powerful impulse to the degeneration and functional weakness of the heart requires no very extensive demonstration; and as a fact, the danger of sudden paralysis of the heart, as of dropsy, occurs earlier and more definitely in those cases of corpulence which from the beginning have more or less assumed the anæmic form of the disease. The *endarteritis deformans* which exists almost as a rule in the corpulence of elderly persons is, besides, a condition which acts in the highest degree as a force embarrassing to the circulation, and should never be overlooked as a source of imminent peril to it from the heart downward. Thus it happens amongst other things, and not seldom, that corpulent persons, when their corpulence has not apparently increased, and where other inimical influences have not perceptibly affected their heart, gradually become dropsical, simply because with advancing age simultaneous progressive degeneration of the arteries has placed an ever-increasing hinderance in the way of the circulation. In other cases the patients die of complications and sequelæ which occur in the course of the corpulence, and stand in more or less definite genetic connection with it. Such malignant complications menace even *infantile* corpulence in the form of extensive catarrh of the respiratory apparatus, and more especially of lesions of digestion (acute and chronic gastric and intestinal catarrhs), as these latter by reason of an injurious influence, which is very active in such cases (improper food), frequently run a longer course, particularly in anæmic corpulence. Greater still is the number of pernicious sequelæ in the adiposity of elderly individuals. Here hemorrhages into the brain, the etiological connection of which with corpulence has been discussed by us more minutely before, must be brought forward as a very frequent cause of death in the corpulent. The sudden death of fat people, of course, depends in many cases upon syncope; but in others, and more frequently, upon apoplexy. At other times, carcinomatous disease, diabetes, etc., kill in a slower manner, by setting up a constantly increasing marasmus, which gradually so completely destroys the previous excessive embonpoint, that only the loose flabby skin over the thin limbs remains as a witness of their former plumpness.

Finally, the corpulent very often succumb to intercurrent affections of all kinds, and especially to febrile diseases. Concerning the reasons of this peculiar malignity of these accidental complications, we endeavored in a former place (see p. 682) to give a more particular explanation; we shall, therefore, now only remark, in connection with what we have said there, that the number of fatal cases from this cause is certainly much greater than that in which a lethal termination is produced by the corpulence itself, or its direct sequelæ. It is, moreover, very worthy of notice that this greater malignity of incidental severe maladies comes to light unmistakably enough, if not so significantly, even in the lower grades of corpulence; and that, regard being had to this state of things, corpulence, even in its commencement, can by no means be looked on as that entirely innocent, comfortable complaint it is often enough regarded as by both doctors and laymen, and even the patients themselves. A short consideration will, however, after the observations already made, make it clear without much trouble, that in times of need, which come upon the individual through stress of severe depressing diseases of all kinds, but especially intense febrile affections, even a small impairment of the power of physiological regeneration may be fatal to the existence of the patient. A diminution of functional power in the tissues, which prevents their undergoing perpetual restitution as regards function, nutrition, and development, by taking up the elements of the blood in sufficient quantity, and thus, always well prepared, defying the devastating storms of disease, is exactly what constitutes the inner idiosyncrasy of the relaxed constitution, just as an immoderate propensity to fat-deposition is what usually affords its principal outward characteristic.

If we mentally glance over all the foregoing remarks about the duration and terminations of corpulence, we shall arrive at the conviction that it is in some measure difficult to speak of a *general prognosis* in this disease. The prognosis will be differently formed according as there is a prospect of full restoration to health or a simple improvement; and besides, both these desirable modifications of the terminations of the disease, in each case, depend on numerous concurrent circumstances.

The *possibility* of an *absolutely favorable* prognosis exists almost alone for the period of lactation; but whether there is any real ground for expectation that the individual case under observation will fully recover, depends on several conditions of different kinds. According to experience, the radical removal of infantile corpulence is most likely to occur when there is no history of hereditary predisposition, when in all probability the disease is principally due to improper alimentation, and when finally there is an external possibility of altering the regimen of the patient in a manner calculated to attain the desired object. If besides we have to do with a comparatively slight degree of the disease, and if this has more of the plethoric character, we may give a favorable prognosis so long as no intercurrent affection of any kind threatens the child.

Cases, on the contrary, where there is hereditary predisposition, or where no ground for the development of the disease can be found in the nature of the food of the child, are less favorable as regards full recovery. The prognosis is also worse when we have to do with an excessive degree of the disease, which at the same time exhibits in a well-marked manner the anæmic type, and finally, when the already-mentioned secondary affections (digestive lesions, rachitis, etc.) which specially characterize the anæmic corpulence of young children are present.

As regards the prognosis in the corpulence of the other periods of life, it is, to draw a conclusion from the observations made already, *quoad valitudinem completam*, unfavorable. The great tendency of the disease to *return* disturbs the prospect of complete recovery. This unfortunate circumstance, however, does not in any wise falsify the fact that *transient recoveries* are pretty often observed, and that temporary *improvements* are still more frequent. The less advanced cases especially admit of such *comparatively good prognoses*, particularly those which, *with no ascertainable hereditary influence*, have unmistakably arisen from the action of some definite *determining* causes, and where at the same time there is a possibility of removing these by a suitable treatment. We here chiefly allude to certain symptomatic forms of corpulence, and of course those idiopathic cases which develop themselves under the influence of too luxurious living with too little bodily activity. The prognosis is, indeed, in these latter cases made worse again by the circumstance that many patients, according to their personal character, are from the first disinclined to comply with the therapeutic rules of moderation, and to give up their improper mode of life, or at least have not the necessary energy to persevere in this. The prognosis is much less favorable where a well-marked *hereditary predisposition* exists, and where further the disease has developed itself apparently spontaneously *without* perceptible determining influence, and at the same time from the commencement exhibits the anæmic character. Now, since cases of this kind occur more frequently in women and elderly persons than in men and younger persons (see p. 634 and p. 635), the prognosis of corpulence, taken as a whole, is less favorable in women and elderly people ; yet it is well in forming a prognosis in particular cases not to take the sexual character or the period of life too exclusively as the standard of prognostic judgment, but to have due regard rather to the general character, and especially the intensity, of the case.

In the latter connection we must expressly mention that the prognosis *in all very advanced cases* must on that account be *comparatively unfavorable*, because the expectation of a spontaneous reduction of the mass of fat is, according to experience, very small, while that of an improvement through any very active treatment is also very precarious. In the section on Therapeutics we shall more particularly speak of the difficulties and dangers with which we have to contend in merely "standing off and on" in favorable cases—that is to say, without producing any definite improvement in the affection, to steer the patient through the unpleasant dilemma of a further accession of corpulence on the one hand, and on the other a rapid loss of strength, with as little injury as possible, by means of a method of treatment more prudent than heroic. The prognosis finally becomes *absolutely unfavorable* when symptoms of functional insufficiency of the heart are added to those of a great degree of corpulence. A livid appearance, with weak, irregular pulse, continual difficulty of breathing, and lastly dropsy, should make us fear a lethal catastrophe, more and more imminent as this complex train of phenomena gradually gets the upper hand after its first appearance and thrusts itself into the foreground of the disease. But even in the earlier stages we should not be too confident as regards prognosis, never forgetting that sudden death from syncope or apoplexy is not unusual with the corpulent (see Terminations), and that further malignant complications and sequelæ may at any moment arise and menace the patient with danger, and that even an apparently innocent intercurrent disorder, especially when accompanied by fever, must be regarded very differently and more seriously than usual, where it occurs in relaxed and fat persons. The tendency of the proposition we made particularly prominent in the introduction to the General Disorders of Nutrition (see p. 278), viz., that the prognosis, in individuals constitutionally affected, who are also suffering from some other disease, should not be made simply according to the habitual character of the intercurrent disease, is probably never more distinctly demonstrated than it is in just these intercurrent diseases of corpulent persons; and it is perhaps never so frequently left unregarded as here. It is, therefore, much to be wished that the physicians of the modern school, with their well-directed endeavors after exact local diagnosis, would, as regards the prognosis of disease, condescend to be led by more general considerations, and would less often omit to make a more complete examination of the general habit of the patient.

Therapeutics.

The *prophylaxis* against corpulence is indeed at present no longer, as in the spring of Greek culture (see p. 608), numbered among the affairs of public hygiene and serious cares of state; yet it may with all justice be now considered as an important part of those private sanitary duties, of which the satisfactory discharge may be constantly laid upon each individual as regards his own person, and upon every one who would be called a conscientious physician as regards that of others. It is further evident in itself that a *rational prophylaxis* against corpulence must rest upon the basis of the pathogeny and etiology of this disease, and must as far as possible strive, when necessary, by little and little to work against the *excess* of those influences which, according to experience (and to some extent in an easily intelligible manner), favor the production of corpulence. But. mark well, *only the excess*, not the influences themselves! For we should, on the other hand, never forget that fat-production, regarded *per se*, is not only not a morbid, but, on the contrary, within certain, though of course elastic limits, a thoroughly physiological process, and a desirable attribute of health. It is only by exceeding those limits that it gradually assumes a morbid character. We can, therefore, in our prophylaxis against corpulence only attempt *always so to regulate the conditions of fat-deposition in each individual, that these boundaries shall not be exceeded; but not to make the conditions of fat-deposition always as unfavorable as possible.* For it is surely not the task of a rational private hygiene with all one's might and at all times to strive after the greatest degree of thinness in oneself and others, merely because it is undoubtedly a good thing to prevent a morbid corpulence!

Since, therefore, what is required for protection against corpulence from the standpoint of health, is the regulation, but by no means the suppression or total destruction, of a physiological process, the question naturally arises, *whether such a prophylaxis is necessary or not for each individual.* It has been shown more minutely in the etiological section of this chapter that the *individual tendency* to corpulence is *extremely diverse;* so much so, indeed, that under one and the same mode of life one man remains thin, while another is perhaps in a condition to produce a quite enormous quantity of fat, or to preserve the greater or less degree of embonpoint he has already attained. We may often go so far as to assert that with not a few individuals, either through hereditary tendency, or through age, sex, temperament, acquired constitution, etc., an immunity against polysarkia exists to such a degree that the deposition of fat, even under external circumstances the most favorable for its production (full diet, indolent mode of life, etc.), will always remain within physiological limits—a prophylaxis against corpulence being, therefore, in such cases quite superfluous. In other cases the immunity is by no means so absolute and lasting, but merely temporary. It gradually diminishes more and more with advancing life, or it passes away prematurely through intercurrent morbid processes (see p. 637). Here the desirability of a prophylactic regulation is manifest, and if possible at a time when the corpulence either does not exist or is but beginning (to some extent *in embryo*). In other cases still the individual tendency is strong—the first signs of the affection show themselves prematurely, not as yet as a severe or really morbid somatic phenomenon, but still as an already clearly recognizable germ of future evil. Here it is evident that the regimen must not only sooner begin, but be of a much more energetic character. If the end, "the preserving of a natural bodily circumference," may be really attained in other cases, here it may unfortunately happen that, spite of the best-advised endeavors, and spite of the most rational mode of life, corpulence is produced *because the individual predisposition to it is too strong*. This non-success of prophylaxis in many cases will surprise those only who undervalue the power of those predisposing influences which are most in question here—heredity, sex, age, constitution, etc.—and who further omit to consider that, besides the known factors which determine the amount of the fat-deposition, quantity of lipogenous materials in the blood, trophic and plastic energies of the tissues, other unknown and less easily investigable causes exist (see p. 628), against which it is frequently almost useless to direct prophylaxis. It may finally be added that too heroic a method of treatment—for instance, a regular starvation-cure, repeated at short intervals—in contending with the higher grades of tendency to corpulence, should be utterly abhorred. Such a prophylactic treatment would indeed finally provoke leanness, and with it certain other somatic changes (sickly marasmus, a great degree of functional weakness of every organ), which, as compared with corpulence, must be regarded as much worse and more dangerous evils. It is therefore as little permissible here as elsewhere—*sit venia verbo*—"to tumble out the baby in emptying the bath" (*das Kind mit dem Bade auszuschütten*).

Where such a well-marked tendency to corpulence can be perceived we should never be too assiduous; at the same time we should be as energetic as possible in meeting the approaching foe in advance; and if we do not always succeed, as before remarked, in driving him entirely out of the field, we may undoubtedly, by means of a prudent prophylactic treatment, at least contribute much towards preventing his becoming very powerful. And here we may lay down thus much in general terms, that:

1. In individuals whose ordinary mode of life involves nothing particularly favorable to fat-deposition (see what follows), an active prophylaxis against corpulence is desirable and hygienically necessary only if any strong personal or temporary predisposition to the disease can be perceived; and.

2. That the measure of the energy to be expended must in general be regulated by the degree of predisposition existing; and finally

3. That we must often renounce a *radical* prophylaxis against corpulence when there is a strong personal predisposition, because under these circumstances such a course is, from other hygienic grounds, inadvisable (see above).

In judging of the propriety or impropriety of a prophylactic treatment, the principal emphasis must therefore be laid upon the individual predisposition to corpulence. Thus, *with a slight natural tendency to the disease*, an active prophylaxis may appear at all events worth a trial, where *an improper mode of life gives a somewhat powerful impulse to the deposition of fat*, and threatens to excite a pathological corpulence in any one. As a general rule, in fine, the prophylactic treatment is naturally indicated in those cases in which that determining impulse just mentioned exists, together with a well-expressed natural predisposition, both influences thus conspiring together. As to general liability, then, it is simply the sum of existing tendencies to fat-production, internal and external, that decides the question in any particular case, the internal being the most important.

In direct connection with our former remarks on etiology, to which we now expressly refer the reader, we may here draw up a category of the individual cases in which, for the reasons already mentioned, there is an indication for a prophylactic treatment.

a. *Individuals with well-marked hereditary tendency to corpulence.*

Notorious corpulence in the parents or more distant ancestors is incontestably an important indication for the early practice of preservative measures against the future, and especially when the habit of the descendants at similar periods of life is the same as or similar to that of their predecessors. It is not at all necessary that in the less predisposed years of childhood and youth the descendants should exhibit signs of any considerable embonpoint. This may have only developed itself in the parents at an advanced period of life. It is quite enough when there is that similarity of figure and of the rest of the somatic constitution which so very frequently stamps all phases of their future temporal existence as the living copy of the previous generation. When the corpulence was in them an attribute of certain periods of life, there is a probability that it will show itself in their children and descendants at similar periods; and naturally also, the more the disease was developed and manifested in the ancestors, the greater will be the necessity for a prophylactic treatment in the descendants.

b. *Women at their climacteric period.*

The stronger natural predisposition to corpulence in the female sex makes a somewhat more extended prophylaxis advisable with them. As, in addition, the climacteric period very often marks the point of time at which corpulence occurs, often comparatively quietly, even in women who were previously thin, the arrival of this period of life requires very particular attention as to precautionary measures against corpulence. We must further remark that the necessity for an active prophylaxis is especially great when, as is frequently the case, the history points to hereditary tendency, and when the female members of the family in an ascending line exhibited a decided liability to corpulence at their climacteric period, or when the signs of a considerable degree of embonpoint existed in the given individual herself (see what follows) in her youth.

c. *Young persons of both sexes with a somewhat well-developed padding of fat.*

The natural tendency to corpulence often makes itself remarkable as a hereditary predisposition even during the period of lactation. It may, in similar cases, either entirely recede into the background during the following years of childhood and youth, the affected individual not being on that account by any means insured against a return of the disease at a more advanced period of life (see above), or a less degree of embonpoint remains present even during youth, so that the hereditary tendency continually betrays itself, from the earliest period upward, by a well-developed padding of fat. In other cases a certain degree of embonpoint occurs gradually in young individuals, at no particular period, from other causes, known or unknown, lending their figure a greater fullness than usually, on the average, occurs in the bloom of youth. Now it cannot at all be expected, for reasons given already (see p. 688), that such a *premature* embonpoint, whether inherited or acquired, will disappear of itself as years pass on. We should rather, on the contrary, take it for granted that on entering the later period of life, in which the predisposition is greater, a continual accession to the fat-padding will take place, and this presumption is fully borne out by practical experience. Here it is evidently worth while to begin early with prophylactic measures, and not to wait for the development of pathological adiposity, all the more when perhaps in a given case there are other signs of a relaxed constitution—for example, torpor of the genital functions, or, in women, an habitual chlorosis, which latter, in connection with the considerable development of fat, must at all events increase in a high degree the suspicion of a natural tendency to corpulence.

d. *Phlegmatic individuals.*

The phlegmatic temperament is probably in many cases one of the phenomena of the relaxed constitution (see p. 638). In others, it may have a more independent signification. At all events, it involves an increased tendency to corpulence, inasmuch as it produces a disposition to a sluggish mode of life. The task here is to paralyze the influence of temperament upon the habits of life of the patient, through suitable prophylactic directions, in such a manner that the disease shall not succeed in developing itself, or, at least, shall be held in check as much as possible.

e. *Sucklings which have been artificially fed on too concentrated or improper substitutes for milk.*

We have already remarked that frequently infantile corpulence may be produced, even where there was probably no particularly strong natural tendency to fat-production, by the method of alimentation chosen. We do not wish, however, to say anything against the extensive use of a well-mixed though concentrated substitute for milk (such as Nestle's Infants' Food). This is only necessary in those particular cases in which, by making use of such preparations in the artificial feeding of a sucking child, there is a continual condition of over-feeding, especially as regards the tendency to fat-production. If this seems comparatively too great, it will be well prophylactically to interfere and employ a less concentrated form of food. On the other hand, all unsuitably mixed articles should be banished from the suckling's diet, especially such as contain too small a quantity of blood-forming constituents (pap, rusk soup, etc.). Their injurious influence often manifests itself, as was mentioned before, in the production of anæmic corpulence, with which at a later period are usually associated affections of other kinds (atonic weakness of digestion, late dentition, rachitis), and which should in no wise be confounded with the healthy embonpoint of normally developed children (see p. 657).

f. *Habitual excesses in eating and drinking.*

The danger of becoming abnormally fat threatens all persons such as are described on p. 643, who, without possessing a personal immunity against adiposity, are accustomed to consume an excess of food, or who, together with a rich diet, imbibe daily a great quantity of alcoholic drinks (brandy, wine, beer). There is no need of much argument to demonstrate the special advantage of a prophylaxis in such cases. The way also which should be taken is mapped out in its chief lines, so much so that any further remarks might appear superfluous. Nevertheless we must, with reference to the most appropriate method of prophylactic treatment in particular cases, make the following observation: That when a Draconic edict of temperance is very improperly hung over the heads of the affected persons, as is occasionally done by physicians, the bodily health of the patients is by no means served, but rather injured.

The foregoing sketch gives at a glance a *résumé* of those groups of individuals for whom a prophylactic treatment of corpulence seems specially adapted; and now that it is fixed, in all essential points, *where* and *when* such a treatment is indicated, we may also undertake to answer the further question, *how* it should be conducted. As natural ways and means of diminishing the tendency to corpulence, the following, described in the section on Pathogeny, present themselves:

1. Diminution of the introduction of lipogenous material in the *pabulum*.
2. Increase of the trophic and plastic energy of the albumenized tissues of the body, especially those of the voluntary muscles.
3. Increase of the general stock of red blood-corpuscles, by promoting their new formation.
4. Increase of the animal process of oxidation, by increased introduction of oxygen.

The prescriptions used from remote antiquity as a protection against corpulence, and best verified empirically, correspond in the main with the aforesaid theoretic requirements, since they range themselves now under one, now under another of the said methods for reducing fat-production, and sometimes under more than one. The choice of these methods and their suitable grouping depend, however, naturally upon *the quarter from which the corpulence threatens to arise in each particular case;* and we must here reiterate the rule that we have already laid down, that it is quite unpermissible to treat all individuals, whose fat-deposition we wish to regulate, in the same manner. We have briefly enumerated the ordinary prescriptions *seriatim*, but, in fixing the order of their succession, we shall not let ourselves be guided by theoretic considerations, because the complex mode of action of these prophylactic agencies does not permit of a sundering of them into distinct categories. In connection with each particular one, we subjoin short *data* respecting its actual or probable method of working, and finally extract from these *data* more particular indications for its practical application.

1. *Regulation of the ingesta.*—A suitable change of diet is

undoubtedly in many cases a very effectual measure to oppose a threatening or commencing corpulence. We shall decide upon a simple restriction of the amount of food taken only when the individual has a notorious tendency to *polyphagia*, and when he has hitherto been accustomed to give himself up without stint to the pleasures of the table. *Yet even in this case the restriction of diet should be by no means absolute, but merely relative*—that is to say, the immoderate indulgence in food *should be reduced* within reasonable limits, and such as alone conduce to health, *but not below the normal measure.* Supposing that we could do what is very difficult to do with most *bon-vivants*, and would require a very powerful authority over his patient on the part of the physician, viz., to produce in a person of that kind even *once*, not to say several times over, an incomplete inanition; he might indeed, as we have before remarked at more length, become thin, but would at the same time be threatened with a loss of physical strength, because the great amount of tissue-change to which he was hitherto subject would no longer be made up for by the accustomed great influx of nutriment. Absolute curtailment of the quantity of *ingesta* has also, as we more particularly showed in the section on Anæmia, a maiming influence upon the vegetative function of hæmatopoiesis—Panum,[1] in particular, having shown that, through often-repeated abstinence, a very considerable oligocythæmia may be induced, because the increase of red blood-corpuscles during the period of abstinence, and during the first part of the following period, is considerably retarded. Now, since we can under no circumstances manage to carry the treatment, by a single or repeated production of inanition, so far in a habitual *gourmand*, because a period must very soon arrive when it will be advisable to feed the patient—who will have become thinner indeed, but, what is most important, much weaker—a little better, it is evident that in such cases a condition of the blood-mass will be artificially produced by the prophylactic method thus adopted, *than which nothing more favorable to the production of anæmic corpulence can be imagined*; for, after the ample manner in which we have already expounded the subject in the section on Pathogeny, it will be easy to understand, without further discussion, that, when there is considerable oligocythæmia, a much smaller quantity of lipogenous material in the *pabulum* suffices to produce a great quantity of fat, than when the blood contains the normal amount of hæmoglobin. In order, then, to protect the merry and careless good-liver from plethoric corpulence, we have directly exposed him to the danger of anæmic corpulence, for which exchange no one surely will thank his physician! But still more often we have to do with this starvation method in the much more numerous cases in which there is no habitual *polyphagia;* and yet, nevertheless, we may either conclude, from the signs already mentioned, that there is a well-marked tendency to polysarkia, or may directly recognize it. In fact, practical experience now teaches us that this starvation treatment, in cases of corpulence of all kinds threatened or existing, is about the worst possible. The temporary thinning is followed by a deposition of fat all the greater and more inveterate, and this, coupled with the phenomena of oligocythæmia (paleness of the countenance, languor, and atony of all the functions), bears witness to the destruction of the constitution which has begun. When, however, it is only proposed to restrict the diet within reasonable limits when it has hitherto been excessive; and when the starvation-cure pure and simple, and at all hazards, is rejected, the reduction of an excessive diet to a normal quantity is surely in suitable cases the first and most important of the modes of treatment to which we can have recourse. Now, the *polyphagia* of confirmed *gourmands* usually has its root in a *polytropia of their taste* (see p. 644); such men eat more than others because they are fond of *enjoying more things one after another*, and because the spice of variety constantly gives a fresh sting to their appetite. It is necessary, here, therefore, in the first place, to diminish the lust of eating by removing one or more courses from the *menu.* By this simple method we may count upon considerably reducing the total quantity of good things enjoyed, even when the patient is permitted to get as much enjoyment as he can out of a smaller number of dishes. It is further advisable not to commence too *brusquely*, but prudently and step by step to undertake the reduction of the bill of fare. We shall arrive much more surely at our goal, if we do not all at once demand from the man who seeks enjoyment from the table great renunciations on the part of palate and tongue, but allow him a certain time to accustom himself to his new and more temperate course of life. But, finally, it is of extraordinary importance, in choosing the articles of diet which may be most unreservedly permitted to the patient, that we should hit upon the best and most suitable; and, since these *qualitative* regulations of the diet must be employed when, with *a natural predisposition* to corpulence, the mode of life of the individual is not intemperate and the diet not excessive, it follows that it must incontestably be of more general importance in the prophylaxis against corpulence than its *quantitative* regulation.

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[1] Virchow's Archiv. Vol. XXIX. p. 241, etc.

What then shall be the chief diet of the person with a tendency to the abnormal development of fat, the problem being to check the tendency *without* injury to his health in other respects? The answer to this question may best be given by the method of exclusion, by a brief comparison between the individual components of an ordinary mixed diet, with respect to their direct or indirect lipogenous properties. We shall then see what articles of diet and what components of them are specially to be avoided, and what others then remain as suitable for habitual diet. That a diet rich in fat is unsuitable where there is danger of corpulence can easily be understood; but the diet-fats in entering the stream of chyle possess not only direct lipogenous properties, by preventing the complete combustion of the non-azotized products of decomposition which are produced from the circulating albumen, but also, as Fr. Hofmann has shown (see "Pathogeny"), have a direct influence upon the accretion of fat, by being packed up unconsumed in the fat-store of the body. This, at least, is the case with the *homologous* fats (see p. 623). In the same way the devouring of a great quantity of the hydrocarbons is to be avoided. These possess the often-mentioned property (see p. 622 and p. 624) of giving a great impulse to the development of fat when they are partaken of in great quantities simultaneously with the fats and albuminates. As to the glutens, Voit's researches (l. c.) have shown that, by virtue of their strong conservative influence upon the organized albumen and that of the circulation, they possess in a less degree the property of protecting the fat already produced from further decomposition. This indirect lipogenous property is, however, much weaker than that of the hydrocarbons and heterologous fats; and as further direct development of fat from gluten is not established, their introduction into the organism where a tendency to corpulence exists, is on the whole of much less consequence than that of the articles of diet already mentioned. It is enough if we take care that they are not partaken of in too great quantities, simultaneously with fat and albumen, as in that case they would certainly give some impulse to the deposition of fat. As to the albumenized materials themselves, there cannot be any question as to any considerable reduction of the quantity partaken of, as a preventive measure against corpulence, since their elements, as we have often said, furnish the very material for the formation and support of the tissues, and are therefore indispensable. Besides this, their withdrawal acts most detrimentally upon the increase of the blood-tissues. It restricts the production of red corpuscles, and thus opens the door to a condition of oligocythæmia which may subsequently, on the employment of a richer diet, act as a powerful auxiliary to excessive fat-production. On the other hand, a highly albumenized diet may surely, *in certain circumstances*, itself directly afford material for the development of a great quantity of fat, since a great part of the fat of the body is undoubtedly produced from the albumen of the diet by the separation from it of the non-azotized compounds. This fat-production from albumen is, however, as we have explained before, the less to be expected the more organized albumen is produced from the albumen of the pabulum in consequence of the trophic and plastic energy of the tissue-elements, and therefore the smaller the quantity of the albumen of the pabulum which is decomposed; and, moreover, the more perfectly the non-azotized products of decomposition are burnt off into carbonic acid and water. If we are careful, on the one hand, to induce a greater storing-up of the organized albumen, and if, on the other hand, we obtain the oxidation of that non-azotized remainder which proceeds from the superfluous albumen of the pabulum, we need not fear an excessive fat-production even with copious influx of albumen, while the organism receives a fitting quantity of the materials which are indispensable for its maintenance. Now, while the development of a considerable quantity of organized albumen from the pabulum may be obtained more easily by means of a different kind than by definite alimentary conditions (see paragraph number 3), the more or less complete burning off of the non-azotized or lipogenous remnant of the decomposed albumen of the pabulum depends upon one essential constituent of the store of combustible material of a different kind, and, on the other hand, more distinctly upon a factor which must be mentioned farther on. The smaller the quantity of this other, above-mentioned, combustible constituent of the diet (fats, hydrocarbons, glutens), the more complete, *cœteris paribus*, will be the combustion of the lipogenous material, and the less will be its deposition in unconsumed form as fat. *A diet, therefore, which contains an abundance of albumen, little fat, few hydrocarbons, and not a great deal of gluten, is best suited to the prophylaxis against corpulence.*

Moreover, the principle just expressed, of which the general correctness is completely proved by practical experience, has in particular cases to undergo manifold modifications and limitations, so as not to forfeit its hygienic utility in other respects, and especially with respect to what other components of the diet may be permitted along with the albumen. We may here in general coincide with the theoretically drawn up rule that the restriction of the introduction of fat, and also of the use of articles of diet rich in starch and sugar, and, in a lesser degree, of such as are rich in gluten, is the more advisable, and should be the more energetically carried out, *the greater the natural tendency to corpulence.* For instance, when this may be regarded as existing, but not in a very well-marked degree, the prophylactic diet, as regards alimentation, should not be too rigorously adopted. Still more important is a second circumstance, which should be carefully weighed in each case before we hastily order any one a too exclusively albuminous diet, either constantly or for a long period. It is, in fact, clear that a very large quantity of albumen is necessary to not only satisfy the trophic and plastic requirements of the organism, but besides, to cover the deficiency of "reserve material," or "material of force" (*Kraftmaterial*), which takes place through the considerable diminution in the quantity of the remaining "conserving" as well as "force creating" constituents of the diet introduced into the organism. An immense quantity of combustible material is absorbed in the development of animal heat necessary for the maintenance of the function of all organs, in order that this in its turn may be maintained in regular course. In the second place, *the functional restitution of the cardiac muscles, etc.*, similarly involves a constant and indispensable expenditure on the part of the blood, which must somehow again be made up, or the "store of force" of the *pabulum* will soon be reduced to an uncommonly low point, which will scarcely admit of any expenditure on *luxury*—for instance, in the form of strong "voluntary movements." Herein consists *one* of the dangers of an exclusively albuminous diet, in the *diminution of that functional capacity for work* (Leistungsfähigkeit) in that broader sense which regards the individual simply as a useful member of human society—that corporeal soundness which permits a healthy organism to undergo a considerable expenditure of force over and above what is necessary for self-preservation, because it always has at its disposal a considerable reserve of energy. Quite in harmony with what we have just said is what has been observed in a great many cases in which, in order to guard against corpulence, the consumption of fats, hydrocarbons, etc., has been reduced to a minimum, and the body nourished almost exclusively upon albumen. Here, sooner or later, a loss of the normal feeling of strength—a very uncomfortable and tormenting sensation of languor and weakness, has supervened, and for good or evil compelled a discontinuance of the prophylactic treatment. A second danger, and one scarcely less worthy of attention, depends on the *incapacity of the digestive organs continuously to digest a sufficient quantity of albumen to meet all organic requirements.* Now, as the development of digestive disorders should never be the effect of a prophylactic treatment of corpulence, there is a clear necessity for a certain prudence with respect to the greatest quantity of

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albumen that should be given as a daily ration; and this should in all circumstances remain in harmony with the functional capacity of the stomach, pancreas, and intestines. Finally, we must bear in mind that a considerable increase in the amount of albumen consumed, with an increase in the production of urea, usually also induces an increase in the production of lithic acid, which, where the tendency to gout which so often accompanies corpulence exists (see p. 679), may further lead to the occurrence of attacks of gout. We may therefore very well ask in particular cases whether it is advisable to replace the bad enemy, corpulence, by the still worse one, arthritis. We must, indeed, have learnt well enough from previous discussion of the subject, that even the regulation of the bill of fare, as regards the quantity as well as the quality of the *ingesta*, should never be carried out too vigorously and in a pedantically one-sided manner. As an important sanitary measure, the following supplement to the principle above expressed, which supplies in its most general form the rule for keeping the diet within bounds, is valuable. Even where we have to do with a well-marked case of corpulence, *the supply of glutens, hydrocarbons and even fats must never be so curtailed as to produce a considerable diminution of the natural feeling of strength and of the functional capacity of the body; and further, the supply of albumen must never be so great that disorders of digestion or signs of the lithic-acid diathesis are produced.*

We give in conclusion a short review of the articles of diet most frequently and most widely used, in such a way as to show: 1. Those which in a prophylactic diet are specially to be recommended, or at least to be permitted without much consideration. 2. Such as should only be used in very moderate quantities. 3. Such as are best avoided, or at least should be only exceptionally used, and then only in very small quantities indeed.

1. The articles of food most *permissible* are: meat broths of ordinary meats, beef and veal (both of them boiled as well as roast), lean ham; of game: venison (red or fallow deer), hare, chamois, partridge, field-fare, red grouse, heath-cock, ptarmigan, pheasant; of domestic fowl: poultry, pigeon, turkey; of fishes: pike, trout (both boiled, but not fried); of other remaining kinds of animal food: oysters and snails. Besides this: green vegetables of all descriptions (asparagus, cauliflower, green peas, beans, spinach, the common kinds of cabbage), prepared in the English or French manner (without fat); acid fruits (raw or stewed).

2. Articles of food which should habitually be partaken of only in small quantities are: *bread*, biscuits, *milk*, *eggs*, *potatoes*, carrots and other vegetables of the like nature (Teltower-, Kerbel-, Kohlrüben), dried husk-fruit, rice, millet, buckwheat, mealy and sweet soups; *sugar*, as an addition to food and drinks (coffee or tea for instance); of animal foods: mutton in every form, beef in the form of beefsteaks, veal as cutlet; of fish: carp; and besides, green salad with oil, and of dessert dishes, wine jellies.

N.B.—The italicized words represent articles of diet widely used, but from their composition ill adapted for the prophylactic method, and here enumerated among those articles which may be used in small quantities only because it would be extremely difficult for most persons to give them up altogether.

3. Articles of diet which should only be used very *exceptionally*, and then only in *very small quantities*. *Butter* (as an addition to bread, potatoes, etc.); *cream* (as an addition to coffee); *fats*, hot and cold; *sauces* (especially hot butter-sauces with fish, mayonnaise with fish, lobster, poultry); of ordinary kinds of meat: pork, etc. (with the exception of lean ham), in every form and preparation; goose and duck; of game: black game (Schwarzwild), marmot, otter, wild duck, woodcock, snipe, quail, ortolan, lark; of fishes: eel, salmon, common trout, turbot; and of other kinds of animal food: crayfish, lobster, frogs' thighs (with their ordinary accompaniment of fatty pastry); all sorts of stuffing (for tame or wild fowl), potato and meat salads, patties (especially *paté de foie gras*), sweet pastry, *confitures*, creams, ices, sweet grapes (and particularly raisins), dates and preserved and candied fruits of all sorts, chestnuts,[1] nuts, and almonds.

2. *Regulation of beverages.*—With regard to the commonest and most widely used of all drinks, *water*, we may say this much, that it at all events has no direct lipogenous influence on fat-production. It can just as little be admitted that the process of animal combustion is at all hindered, and an indirect impulse thus given to fat-production by the introduction into the system of a great quantity of water. The use of water is therefore unrestrictedly permitted to the corpulent by some authors (especially Harvey and Banting). Others, on the contrary (such as Daniel), recommend curtailment as regards water, and the use of dry and compact articles of diet, as an effectual method of prophylaxis

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[1] Xenophon (Anabasis, Book V., Chap. IV.) relates that in the barbarous nation of the Mosynoikoi, on the Pontos Euxinos, the children of the chiefs were fed with chestnuts to make them beautiful, which developed such a padding of fat on them that they appeared to be almost as broad as they were long. Such crammed children were shown to the Greeks, as they marched through under Xenophon's leadership, and the Greeks in this campaign first learned to know and prize sweet chestnuts as an article of diet.

against a well-marked tendency to corpulence. The statistics by which Daniel supports his recommendation are not fully conclusive as regards the men and animals (horses) experimented on, because a diminution of the quantity of water introduced into the system makes the body at all events poorer in water, and therefore absolutely lighter; and the observed reduction in the weight of the body can certainly not be entirely attributed to a reduction of the quantity of the fat of the body. Nevertheless, it is intelligible that a long-continued treatment by thirst, such as Schroth's, for instance, must have rather a hindering than a favoring influence upon the deposition of fat, and will, as a rule, lead to real thinning; but, by cutting off the supply of water, the appetite for solid food soon disappears, and the thirst-cure finally becomes nothing more nor less than a hunger-cure! For the same reasons, therefore, as led us before to express ourselves against the utility of an absolute restriction upon diet, we must now declare against the cutting off of the water supply, since, as we have repeatedly remarked, the production of marasmus and anæmia should not be the result of a prophylactic treatment of corpulence.

Of ordinary warm drinks of a non-alcoholic nature, *coffee* and *tea*, with a small quantity of milk and sugar—or, better still, without such an addition—may be permissible in moderate quantities without much hesitation. A great quantity of strong tea or coffee is, on the other hand, on other accounts, highly detrimental to the health, and may also indirectly favor the development of corpulence, since there is some reason for attributing to them a retarding influence upon tissue-change. On the other hand, *chocolate* or *cocoa* should under all circumstances be avoided as habitual drinks by such as bear in them the seeds of corpulence, or already exhibit definite signs of the disease. The considerable amount of hydrocarbons (and frequently fat also) in both beverages makes them quite unsuitable when our object is to protect against corpulence.

From the eminent importance which alcoholic drinks have unquestionably possessed from time immemorial in the civilized life of most peoples, and still possess in the daily household life of innumerable private individuals, the regulation of their consumption where corpulence is threatened is often of scarcely less importance than the surveillance of the diet. In any case, the abuse of alcohol, for other reasons which we shall not here particularly specify, is injurious to health, and to be reprobated; but when we have to deal with the avoiding of corpulence, it is especially deleterious even where the tendency to this is but slight. The daily use of even a small quantity of the stronger alcoholic drinks (brandy, liqueurs) is most decidedly to be advised against, just as that of a great quantity of wine and beer; for in both cases a comparatively large amount of alcohol is daily taken, and this substance, like the hydrocarbons and fats of the food, possesses in a very great degree the property of preserving the already formed fat of the body from undergoing further decomposition. Beer, which is ordinarily so widely used as a drink, is rightly held in particularly bad repute in the prophylactic treatment of adiposity, as it more easily than any other alcoholic beverage provokes an immoderate consumption, and contains abundance of hydrocarbons (dextrin, malt-sugar), as well as alcohol. We should, therefore, wherever we have to interfere for the prevention of approaching corpulence, permit the use of wine only, and this in very great moderation. Among the different wines, those kinds which are rich in alcohol and at the same time acid are only permissible for daily use much diluted with water. Those which are strong and also sweet are to be rejected under all circumstances. The lighter acid wines, such as Bordeaux, are best tolerated, being comparatively the least injurious; and to such as cannot give up the use of alcohol, or are afraid to do so altogether, a small quantity freely diluted with water may daily be allowed either in the middle of the day or in the evening. For it must here again be declared that the prevention of corpulence is not to be regarded as the one chief object of hygiene; but that frequently, where there is an individual predisposition to corpulence, it may be, for other reasons, necessary and salutary to exhibit alcohol daily in the form of a little wine, and that under such conditions we should not be too shy of now and then in due course letting stream through the organic machine that beneficial and refreshing agent in which the faith of mankind has, not without reason, from time immemorial suspected and honored a veritable "godlike" power.

In connection with what we have just remarked with respect to alcohol, let us here add a few words about another article of luxury, namely, tobacco. We do not think that moderate tobacco-smoking, such as alone merits the name of a hygienically permitted luxury, has any considerable influence (adjuvant or the reverse) upon the process of fat-production; and accordingly, where there is a tendency to corpulence, we think that there is just as little indication for forbidding it as there is for zealously recommending it. When, on the contrary, English and American physicians have celebrated *tobacco-chewing* as a very efficacious prophylactic against corpulence, and prescribed it, we can by no means coincide in such a recommendation in any case, since this nauseous habit can scarcely in our opinion act in a limiting manner upon the deposition of fat otherwise than by undermining the appetite, and, by setting up a chronic dyspepsia, provoking a certain degree of marasmus. The same holds good, and perhaps in a still higher degree, of other customs and vices, such as the habitual use of the preparations of *coca* and *haschish*, and of *opium-smoking*, and above all, of that senseless and injurious *misuse of morphia in subcutaneous injection*, which latter fashionable vice is, as we know, at the present day so much in vogue that in some places, and especially in medical circles, it is looked on as quite the mode to be a slave to it!

3. *Stimulation of the activity of the muscles.*—We have already in the section upon Etiology referred to the great importance of the function of the voluntary muscles in *lipogenesis*, and shown why vigorous muscular action antagonizes the extreme deposition of fat (see p. 646). As may be remembered from that description, muscles, when methodically exercised (that is to say, not too violently, and with regular pauses for rest interrupting their activity), are stimulated not only to increased functional, but at the same time to increased nutritive and plastic activity. They increase in circumference and mass, and soon become hypertrophic, by storing up and fixing in themselves additional chemical matter, and particularly albumen. Now since, moreover, the muscular function, in so far as it differs from the vegetative function, is for the most part under the control of the regulating direction of the will, its vigorous voluntary exercise furnishes a very suitable means, which is not to be superseded by any other, for secreting organized albumen from that in circulation, or, to express it in a somewhat different form, to limit the decomposition of the circulatory albumen and the secretion of fat. But

besides this there is also, as a similarly important factor in the prophylactic value of bodily movements, the increased amount of oxygen taken up during their continuance, in consequence of which the lipogenous material present in the blood, or in process of development, will much more easily undergo a further oxidation to carbonic acid and water, and will be much less liable to be transformed into true corporeal fat. Finally, it is also very probable that increased action of the muscles within certain limits has a favorable action upon hæmatopoiesis, that is to say, has a stimulating influence upon the new formation of red blood-corpuscles, and this makes fat-production more difficult in proportion as it remedies an existing oligocythæmia.

We may, therefore, under all circumstances recommend individuals with a tendency to corpulence, who are at the same time unrestricted in the use of their limbs, a considerable amount of daily exercise; always remembering that not merely the muscles of the lower extremities, but the other muscles also should as much as possible take part in the nutritive and plastic stimulus (or that the tendency to flesh-production should be as much as possible equable). It is therefore, for example, very advisable to set persons with a tendency to corpulence, which produces a tendency to sluggish bodily habit, to take daily walks, to let them undertake frequent and rather long journeys on foot, and to skate in winter; but, still better, in addition to keep them to swimming, rowing, and gymnastics, because in these latter motions the muscles of the upper extremities are also called into vigorous requisition. Just, however, as the carrying out of prophylactic prescriptions with regard to food and drink must undergo certain necessary limitations, the development of motor power should not be carried to an unreasonable degree. A moderately energetic excitement of the voluntary mobility, not a galling overtasking of the strength, is what is most healthful and salutary, and what in all cases should be aimed at. It is, however, most important, in dealing with elderly individuals who have a tendency to corpulence, to warn them most strictly against all excessive bodily exertion, since this, where that frequently existing form of morbid change in the vessels (*endarteritis chronica*) is present, would directly expose the corpulent person to the danger of an apoplectic attack. It is thus here also as necessary to treat each case most carefully on its own merits, as to exercise a constant supervision over it, in order, without otherwise endangering the health, not to exceed the right measure for the prophylaxis against corpulence, but, on the other hand, really to reach this.

4. *Other dietetic prescriptions.*—Hippocrates himself recommended for all such as wished to remain slender and not become fat, in addition to moderate and little substantial food and much exercise, a light clothing and long tarriance in cool air with nude bodies, and, finally, cold washings and baths (see p. 609). Similarly at the present day, when a tendency to corpulence exists, hydriatic proceedings are among the favorite prescriptions: cold affusions and drenches, and also daily cold baths (in summer in the open air, in winter, if the opportunity of the dwelling-place admits, in enclosed swimming-baths, or in the tub). There can, indeed, be no doubt that the powerful stimulus which the general tissue-change receives from such cold applications to the external skin, and which betrays itself during these by quickened respiration and increased development of carbonic acid (Liebermeister), has a beneficial influence upon relaxed constitutions, and is at least not favorable to corpulence. In this manner dietetic ordinances of this kind, combined, with a suitable diet and proper prescriptions as to bodily exercise, into a general plan of treatment, must certainly, with justice, receive the same attention from a rational standpoint as was extended to it from time immemorial by medicinal empiricism, and must, therefore, always be named in common with the other already enumerated methods of protection against corpulence in treating of the prophylaxis against this. Finally, we may mention that, in the "good old times" of the middle ages, an industrious use of the sexual function was the prophylactic measure recommended as at their disposal against threatened excessive corpulence in certain chaste professions. How far the modern physician and the continent man who is in need of this form of prophylaxis, may come to an agreement to recommend or to make use of this prophylactic, we leave, in equity, to the moral judgment of the parties concerned.

We have expatiated thus widely in our prophylactic notes because, in our opinion, the difficult point of the general treatment of the morbid condition in question lies in the preventing of it, and because those remedies which must be especially adopted, when corpulence is already present, to get rid of it, must be mentioned and described even when dealing with prophylaxis. Indeed, in the special therapeutics of adiposity, into which we shall now go, we shall be able to treat of many important points with great brevity, and on the whole shall have but a few small additions to make which may be regarded as desirable supplements to the plan of treatment when the disease is well marked.

The *indicatio causalis*, in cases where the disease is already present at the age of lactation, demands in the first place a change of diet (see above); and if the adiposity is of a specially anæmic type, preparations of iron should be given at the same time, and this we usually order in combination with phosphate of lime (saccharated carbonate of iron, two and a half drachms; phosphate of lime, half an ounce; white sugar, one ounce; make into a powder, of which as much as can be held on the end of a knife-blade is to be taken three or four times daily).

The use of iron is no less earnestly to be recommended in all anæmic forms of the corpulence of adults, whether *idiopathic*—from hereditary predisposition, influence of sex, period of life, etc., or *symptomatic*—in consequence of chlorosis, loss of blood, etc. We give in all such cases either the Bland-Niemeyer pills, to which we gave special preference in describing the treatment of anæmia and chlorosis (see the corresponding chapter), or chalybeate mineral waters (from St. Moritz, the Pyrenees, Driburg, etc.), which may be drunk systematically at home or at the watering-places themselves, until the anæmic color is improved. In those cases of corpulence, moreover, in the history of which dietary intemperance has evidently acted a part as an essential etiological force, an appropriate reduction in the quantity of food, a simplification of the bill of fare, and a suitable choice of permitted dishes, according to the rules given in the section on prophylaxis, must be insisted on. The abuse of alcoholic beverages, when this is evidently a cause of corpulence, similarly demands appropriate measures for the reform of the bad habit. We need not here call particular attention to the difficulties which, in many cases, attend the treatment of habitual topers, and even of more moderate drinkers, and which have their principal root in the reduced moral energy of these individuals. On the other hand, we must expressly notice the fact that, in dealing with the intemperate use of alcohol, we must always proceed slowly and gradually, for, as we know, an attempt at sudden and violent suppression of the habitual appetite may easily be followed by dangerous attacks of nervous irritability (*delirium cum tremore*), with subsequent collapse. It will, moreover, scarcely be deemed advisable, when gradually diminishing the daily allowance of alcohol, to proceed to entire withdrawal of the stimulant, since, for most patients, even after such treatment, a certain moderate amount of alcoholic beverage remains necessary to enable them to display a fair amount of activity and to attend to their business.

In the choice of the particular form of alcohol to be still allowed, we must bear in mind the differences between the various spirituous drinks noticed in speaking of etiology and prophylaxis. We should, therefore, above all, forbid the use of brandy and beer where this has been immoderate, and gradually replace them by a moderate quantity of wine. Finally, in those corpulent individuals who apparently partly owe their illness to a sluggish mode of life, particular attention must be directed to the excitement of muscular activity. In such cases it is sometimes a good thing to engage the intellectual attention of the patient in plans and undertakings, for the carrying out of which a great deal of bodily activity and a renunciation of his former phlegmatic mode of living is unconditionally necessary!

The measures for the etiological treatment of corpulence just alluded to will be serviceable in preventing the further progress of the disease in all those cases in which it has developed itself under the influence of distinctly perceptible noxious agencies. They will, in many such cases, have a truly radical effect, especially when the corpulence has not attained any very considerable degree, when the natural tendency to it is not very strong, and when, therefore, the conditions are particularly favorable for its complete removal by a mode of treatment directed against its cause.

In more advanced cases, on the contrary, in which the natural tendency to the disease has from the first shown itself considerable, the affection having developed itself apparently spontaneously without perceptible determining causes, an *essential* treatment of the disease must be adopted. The means and methods adapted to the indications furnished by the symptoms are, indeed, for the most part, not essentially different from those spoken of in the section on prophylaxis; but they must, as a rule, be now employed more energetically, more regularly, and for a longer period than when the problem was simply the prevention of corpulence. There are, however, some other methods of treatment which now have to be considered, but which we usually abstain from employing until the occasion for them arises—viz., when the corpulence has distinctly developed itself.

The best and most approved *dietetic* treatment for the diminution and removal of the higher degrees of corpulence is that invented by Harvey, first tried with good results upon W. Banting, and christened after the latter as the "Banting System" (l. c.). This is at bottom only a particular species of the treatment of corpulence, or the predisposition to it, by rational alimentation; but, at the same time, a form of which, as well from the strictness as from the conciseness of its rules, is especially to be recommended where a rigid carrying out of the dietetic principles already developed seems most particularly desirable. This method of treatment chiefly owes its universal fame to the very original and delightfully humorous style of Banting, who in his "Plain Letter to the Public," after a graphic sketch of the inconveniences he had endured, reported the happy cure of his corpulence by Dr. Harvey, and not only presented this latter with a well-merited garland of honor, but immediately procured for the system adopted by him most general social recognition. "Bantingism" thus actually became within a short time, not only in England but on the Continent, a species of modern sport, in which every distinguished personage with the smallest suspicion of a tendency to corpulence wished to take part as a matter of duty, because it had become quite the fashion, and was a matter of *bon ton.* In the lapse of time it is true that certain evils of the Banting system have come to light, which have to some extent diminished the sanguine hopes entertained concerning it. The excitement of novelty has besides gradually abated, and the method is therefore less the rage than it was at first. Spite of all this, however, the method of Harvey must always be described as a very valuable addition to the rational dietetic treatment, and must accordingly occupy a very prominent place in the future. Even now the physician who has just come across a case of somewhat advanced corpulence must at least ask himself the question whether a Banting cure be not the best thing he can order his patient.

The particular articles of daily diet, as drawn up by Harvey in the case of W. Banting, were as follows:

[1] "For breakfast, at 9 A.M., I take five or six ounces of either beef, mutton, kidneys, broiled fish, bacon, or cold meat of any kind, except pork or veal; a large cup of tea or coffee (without milk or sugar), a little biscuit, or one ounce of dry toast; making together six ounces solid, nine liquid.

"For dinner, at 2 P.M., five or six ounces of any fish except salmon, herrings, or eels; any meat except pork or veal; any vegetable except potato, parsnip, beet-root, turnip, or carrot; one ounce of dry toast, fruit out of a pudding not sweetened, any kind of poultry or game, and two or three glasses of good claret, sherry,[2] or madeira —champagne, port, and beer forbidden; making together ten to twelve ounces solid, and ten liquid.

"For tea, at 6 P.M., two or three ounces of cooked fruit, a rusk or two, and a cup of tea without milk or sugar; making two to four ounces solid, nine liquid.

"For supper, at 9 P.M., three or four ounces of meat or fish similar to dinner, with a glass or two of claret or sherry and water; making four ounces solid, and seven liquid.

"For nightcap, if required, a tumbler of grog (gin, whiskey, or brandy, without sugar), or a glass or two of claret or sherry."

Under this form of diet, which Banting adopted for a year (from August, 1862, to August, 1863), his weight fell from 202 pounds (=14 stone, 6 pounds) to 156 pounds (=11 stone, 2 pounds), that is to say, nearly one pound per week, or forty-six pounds within a year, the circumference of his body at the same time diminishing about twelve and one-quarter English inches. At the same time there was improvement in his general health, greater ease in bodily movement, especially in going up stairs, etc.

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[1] Extracted from Banting's "Letter on Corpulence Addressed to the Public." Fourth edition. London, 1869.

[2] Banting says, in the preface to this edition, that though formerly speaking of sherry as "very admissible," he had since discovered that "it promoted acidity."

The reduction of the corpulence was a radical one to this extent that Banting, after seeing his weight and bodily circumference nearly approaching the normal standard, for the sake of experiment returned for a while to all forbidden foods and beverages (except beer), without suffering from a return of the corpulence.

J. Vogel, in his useful treatise on Corpulence (l. c.), has tried to arrange Harvey's bill of fare in a manner more conformable with German usages, and proposes the following regimen as a suitable one for the removal of corpulence when present:

1. Breakfast: Coffee without milk or sugar, or with but a small quantity of both, a little toast or biscuit (no butter, no cakes).
2. Second breakfast, for persons accustomed to high feeding: two lightly boiled eggs, a little raw lean ham, or other kind of lean meat; one cup of tea, or one glass of light acid wine.
3. Dinner: One plate of thin meat soup, lean meat (boiled or roast), green vegetables, or *compot*, a few potatoes, and a little bread.
4. After dinner: *Café noir*.
5. Supper: Meat soup, or tea with cold meat, lean ham, lightly-boiled eggs, salad, and a little bread.

Both these schemes—Harvey's original one and that imitated from it by Vogel—on the whole conform to the requirements of dietary through which the further deposition of fat shall be limited as much as possible, and the already stored-up fat gradually used up. In both, also, this end is attained in a similar manner, namely, by the greatest possible diminution of the consumption of fats and hydrocarbons, with, at the same time, the introduction of a considerable quantity of albumen. Harvey's treatment is, as any one may see by comparing the two, by far the more consistent and the more precise; and since, in dealing with persons of a firm will, much in a prescription depends on this latter character, the English method is, and will remain in many cases, much the more practically serviceable. It also gives the physician a guide-post which will serve to direct him as to how he should proceed where he finds occasion to make certain changes in the dietary rules in particular cases. He must, in fact, in all circumstances strive after that numerical precision which constitutes the one chief excellence of the English Banting cure, and must clearly prescribe to the patient, by weight and measure, *how much* he may and shall daily consume of each particular article of food and drink!

The quantity and quality of the *ingesta* must, however, principally depend upon *how the patient bears the treatment;* whether, on the one hand, a considerable diminution of the corpulence has been attained with a diet of this concentration, or whether, on the other hand, morbid symptoms may not have developed themselves during its progress, which indicate the necessity of some change in the way of relaxation of the rules. If such symptoms develop themselves early and with great vigor during a punctilious carrying out of Harvey's prescriptions, the desired effect upon the weight of the body can certainly almost never be looked for, though a temporary reduction of the corpulence may almost certainly be reckoned upon. On the contrary, in many cases in which a pure Banting cure, according to Harvey, has been adopted, unpleasant effects occur sometimes very soon, sometimes at a later period, which ought not to surprise us with such an exclusive dietary.

In fact, all the disadvantages that may easily attend an almost exclusively albuminous alimentation, as we have pointed out already (see section of Prophylaxis), are particularly liable to occur in a high degree as a logical result of the Banting system; and by no means all corpulent persons are like W. Banting in the fortunate position of being able to submit to the stern demands of the system for many months together, with health otherwise undisturbed. Not a few patients, who have at first joyfully undertaken to carry out the treatment, in the hope of being freed from their enormous load of flesh, feel themselves after a while so weak and miserable that, although the weight has somewhat diminished during the period, they have to petition earnestly for an interruption of the cure. Others conceive a temporary insurmountable aversion to the meat regimen, or suffer from dyspeptic troubles which make a further carrying out of dietary treatment impossible for the time, and make it a difficult matter even in future. We are therefore personally of opinion that it is best to avoid the evils thus indicated from the outset, and that in ordering a Banting cure, care should be taken to interrupt it temporarily at suitable intervals, so that it may not be employed continuously for a long period, but rather interruptedly (staccato fashion). If care be also taken not to prolong each period of treatment until any considerable feeling of weakness or distinct dislike to the diet, or dyspeptic symptoms are produced, the physician has the great advantage of being able, during the period of treatment, without other ill-effects, to let the full vigor of the treatment bear sway. Suppose, for instance, when a patient is personally very anxious for the reduction of his abnormal fat-padding, or when his corpulence has reached troublesome dimensions and produced threatening symptoms (particularly connected with the heart), we cause him to adopt a rigid Banting regimen for one or two weeks at a time and several weeks in succession, allowing him, however, in the intervals a period of rest of four to eight days, during which he partakes of a smaller quantity of meat, but a larger quantity of hydrocarbons and fats (in the form of bread, milk, eggs, potatoes), thus storing up fresh power for further efforts; we shall bring the patient near the desired goal more slowly, but much more surely, and with less danger by this method of proceeding than by imprudently and perseveringly forcing on a Banting cure which, in the long run, would be extremely trying. We have, indeed, had so much reason to be satisfied with the modifications of this treatment just explained, in some cases that have come under our observation and treatment within the last year, that we do not hesitate here most earnestly to recommend others to try it.

In the regulation of such an interrupted Banting cure we should take care not nly to estimate the weight of the patient repeatedly during each period of treatment, but to check it properly during the intervals of rest. In no case should it gain reach the point at which it stood before the commencement of the preceding eriod of treatment. By prudent regulation of diet during the interval, it is genrally possible to produce the desired recovery in the patient without allowing the eight essentially to increase.

Besides the proper modification of the diet, according to the rinciples and methods described, care for proper bodily exercise urnishes a further important therapeutic task where corpulence present. Whilst we must refer the reader to what we have said on this subject in the sections on etiology and prophylaxis, we shall here only observe that the *practical carrying out* of the ordinances, which have for their end an increased stimulation of muscular activity, is often impeded by difficulties of all kinds, and should always be carried out with a certain amount of prudence. Not to speak of the discomfort of patients to whom comparatively insignificant bodily movements are a torment, because they immediately fall into copious sweating, soon become tired, and suffer from a feeling of oppression (see p. 674), *the danger of an acute over-exertion of the heart with rapid consecutive lesion of its muscles*, should never be entirely overlooked. The heart, which in the higher degrees of corpulence is usually surrounded by a thick layer of fat, and even interpenetrated with fat, is in consequence of these anatomical changes, as we saw before, functionally disordered in a great degree, while it is but little fitted for constant energetic action. If now, in consequence of vigorous bodily movement and exertion, a momentary over-excitement of the heart-muscles should occur, acute paresis, or even acute lethal paralysis of the heart, may be the sorrowful consequence of such an excess, as indeed the attacks of syncope, which often so suddenly occur in the corpulent, teach us. We have also, in our prophylaxis, to think of another danger, namely, that of *rupture of a cerebral vessel* with a *fatal apoplectic seizure*, since where that atheroma of the arteries, so common in elderly individuals, is present, it may afford a contraindication against too great bodily exertion. If the anatomical changes in the heart that we have described do not as yet exist, we have to do with a case in which the corpulence itself is not very far advanced. In all circumstances *prudence* is advisable, and the vigorous, fatiguing forms of bodily exercise we have already recommended as a treatment for corpulence—mountain-climbing, skating, swimming, rowing and gymnastics—should only be employed with *young corpulent patients*, whose arteries are as yet not rigid or abnormally fragile; and even among these younger individuals only in those *whose adiposity has not reached any very great degree*, and who possess *a sufficiently powerful pulse and a competent and sound action of the heart*. With all other corpulent persons, on the contrary (elderly individuals, and extremely fat men with bad pulse-character), the aforesaid forms of motion are quite contraindicated and frequently dangerous, inasmuch as they are of altogether too violent a nature.

In order, however, that in cases of this latter kind the patient may not leave the important territory of voluntary motility altogether fallow, that a curative agent so undoubtedly influential may not be altogether neglected, care must be taken that the corpulent person take daily *as much* bodily exercise as he can without *danger to himself;* and that, further, he should *take such exercise as shall cause the least possible distress to the heart.* Slow but long walks upon the level, a proper amount of riding and billiard-playing for those who have been already accustomed to these pursuits and who have regularly kept their hands in ; finally, the gentler kinds of chamber gymnastics are a form of bodily exercise which may generally be permitted even in the higher degrees of corpulence, though not without particular consideration, and which we should not neglect expressly to order where we are compelled, for reasons already mentioned, to abstain from more energetic measures. We can see therefore that the simple precept that fat people should take good care of themselves as regards their bodies, should be set forth in all particular conditions; and it is certainly by no means superfluous on the part of the physician in each individual case clearly to determine and prescribe even the measure and form of the exercise to be taken.

While the curative measures hitherto considered are principally adapted for common and daily employment, and are essentially of a dietetic nature, there are others farther removed from this commonplace region, which bear on their faces an exceptional, or, if you please, medicinal character in the widest sense of the term.

The treatment by certain medicinal waters rightly occupies the first place in popular favor as a curative method in commencing, and as a palliative method in advanced corpulence. We may mention, among the first rank of these, the *alkaline springs of Marienbad and Tarasp*, the waters of which are drunk by patients either during a single visit, or better still, annually.

The waters of low temperature, and containing Glauber's salts and sulphuric acid, are also rich in bicarbonate of soda, and owe the greater part of their universal celebrity to the circumstance that at these watering-places so many fat people every year find their trouble diminished or removed, and can go home after a few weeks' use of the waters considerably slenderer and several pounds lighter.

A morning promenade at Marienbad, in the neighborhood of the Kreuzbrunnen, will abundantly convince even the non-medical spectator of the world-wide fame of this watering-place, as regards the cure of corpulence—so great is the crowd of Sileni and Falstaffs from every land which assembles there betimes every morning during the season, to walk slowly to drink the prescribed number of goblets of the healing waters, and by and by to betake themselves with more hasty steps to those elegantly-built houses which lie concealed among the shrubs of the Curpark, and which are dedicated to the mightily compelling "necessities of nature."

If in the treatment of corpulence we give the *crenæ* (or cold springs) containing Glauber's salts the preference over the *thermæ*—Marienbad, for instance, over Karlsbad, which lies near it—this is principally on account of the possible danger of apoplexy or syncope which is to be feared from the strongly stimulating and over-exciting effect of the hot mineral water on the heart; while that purgative effect which we desire above all is a property possessed just as much, or in fact in even a higher degree, by the *crenæ* (Marienbad, Tarasp) than by the thermæ (Karlsbad, Vichy). Now it seems to us highly probable that the laxative effect of these mineral waters plays a very important part in their so decidedly curative influence upon corpulence. At all events, at these watering-places we observe that, as a general rule, the more powerfully the spring "works" upon the patient—that is to say, the more copious the pappy evacuations which daily occur after drinking the "Brunnen" during his promenade—the quicker he gets rid of his excessive fat-padding. Whether the bicarbonate of soda which these springs contain in great quantity, in addition to the purgative Glauber's salts, exercises any decided action upon the corpulence, as was formerly believed, or whether the mixture of this salt simply has the desirable effect of rendering the long-continued Brunnen cure more endurable and less irritating to the stomach, as we are personally inclined to believe, we shall now leave undiscussed. At any rate, the decidedly cathartic effect of the Brunnen cure in Marienbad and Tarasp is what we always have most particularly to reckon upon when we recommend it. Since, however, it has been proved by Radziejewski's beautiful researches, that the purgative effect of Glauber's salts and other salines principally depends upon increased excitement of the peristaltic motion of the intestines, and that the evacuation which occurs after the use of neutral salts contains a great quantity of peptones from the small intestines, and also much more fat than normal fæces, these matters apparently not having time to become absorbed, owing to the peristaltic storm, such a Brunnen cure in Marienbad and Tarasp must assuredly be regarded simply as a starvation-cure with all its advantages and disadvantages. It is further clear, however, that these purgative mineral waters, as therapeutic agents in corpulence, are in the right place *where a moderate amount of starvation is indicated*—therefore, in the *plethoric corpulence* of good livers, who, while using but little exercise, take an immoderate quantity of food and a fair share of beer or wine, thus gradually becoming fat by a method pursued frequently and by many persons. Here, however, the Brunnen cure incontestably affords an eminently approved means of remedying the false relation between supply and expenditure, or even gradually to turn the tables, even if we confine ourselves, in quite one-sided fashion, simply to the cathartic action of the alkaline waters, without allowing the other accidents of the "cure," the prescribed diet, and the regular exercise in the fresh air, to enter into the computation. For, even if we take for granted that the patient will go on indulging in his luxurious manners of life during his use of the spring, he must, thanks to the laxative effect of the mineral water he daily drinks, regularly lose again *per anum* a considerable portion of what in his criminal excess he has introduced *per os*, thus being in a certain sense like the sieves of the Danaïds!

But there is another circumstance which helps to make the fortune of the "Brunnen cure," where this is pursued in the locality of the spring itself, namely, that it usually forces even the most hardened swine as regards the pleasures of the table to make some halt and to undergo a temporary repentance, because happily among the public of each particular watering-place the most terrible legends of the evil consequences of errors in diet, overloading of the stomach, etc., told on the authority of eye-witnesses, are always going the rounds, and are even industriously fomented by the physicians themselves. The desire of life and fear of death, as well as the good example of others, and above all the bills-of-fare of the hotel, rigorously kept within the limits of the rules of treatment, compel to unwonted temperance many a guest who at home would have found it difficult to abjure his vices, or to keep them sufficiently in check. Besides, it need not be concealed that any considerable departures from the usual diet of the Brunnen (quantitative, or worse still, qualitative) are in reality almost always quickly punished by unpleasant morbid symptoms, such as colic and smart diarrhœa ; and although these phenomena are generally not of a character that involves danger to life, they are very effectual monitors to the imprudent debauchee, who thinks he has in these each time a warning "*memento mori.*"

If, however, we look a little more closely and attentively into the much talked-of Brunnen diet, we must not only grant that it possesses the negative excellence of forbidding all food difficult of digestion and calculated to produce flatulence, but allow it an important part in the positive effect of the cure. The Brunnen regimen either proscribes altogether the use of alcohol, or limits it in each case so far as is possible and advisable—a circumstance which surely fulfils an important indication in all cases of corpulence, and in many withdraws the cause of the disease; and which, therefore, is certainly not lightly to be excluded in summing up the results of the entire "cure." In forbidding butter, as well as fat foods and sauces, the Brunnen diet comes very near that of the Banting system, to which it is also very similar in prescribing meat-soups, lean meat, and green vegetables not likely to produce flatulence, and a little stewed fruit and bread, as the articles most suited to the table during the "cure." In forbidding raw fruit and all acid food (salad, for instance), it goes farther than the Banting system, though essentially only on the ground that the use of this article, while the patient is drinking the water, is especially liable to cause colic. On the other hand, the granting of milk, amylaceous and sweet food, is rather more free than in the Banting system. All things considered, we must, however, recognize the fact that in closely following out the dietetic rules handed down from former times, the corpulent guest decidedly fares well as regards the proposed end of his cure, not only because he is by this means most surely spared dyspeptic attacks of an unpleasant kind, but because on this diet he daily assimilates a comparatively small quantity of fat-producing material with a sufficiently large amount of blood-producing food. If, finally, we mention the diligent walking exercise which forms a part of the before-described obligations of residence at the spa, we at least arrive at a complexity of healing agencies, in which indeed the water of the spring is the most important single factor, but in which the influences, taken together, bear a less conspicuous part in the favorable results in so many cases of this kind. It is at the same time evident that the full blessing of the Brunnen cure can only be enjoyed by those corpulent persons *who undergo it at the place itself*, and if possible *return thither year by year*. Thus only is it possible to bring to bear all these other powers in their totality, as is desirable in the interest of the patient, and as may there be done without demanding from him too great self-control. A Brunnen cure undertaken with water sent to the home of the patient is usually but a half measure, for the simple reason that the magical power of interdiction resident in the life of the watering-place is wanting to make the strict carrying out of the necessary dietary prescriptions a comparatively easy duty for the patient.

Now, while in cases of plethoric corpulence the repeated and copious use of the alkaline *crenæ* is specially indicated as a method of treatment, and should be strictly recommended, in cases of *anæmic corpulence* this is usually quite too heroic a method. Pasty individuals, whose pale countenances and habit in other respects lead us to conclude that in all probability a certain amount of oligocythæmia is present, at any rate feel themselves, as a rule, after a short use of great quantities of this strongly purgative mineral water, extraordinarily languid and exhausted—to such an extent that it is often rightly thought necessary to give up exposing them to the further weakening effects of such a "cure." This evil consequence may be partly avoided by causing them to drink the water in but small quantities daily, while their diet is richer, the cure being thus extended over a longer period, or, better still, by choosing alkaline waters of which the laxative effect is slighter, while they contain *iron*, and therefore possess distinctly tonic properties. Franzensbad, Elster, Kissengen, etc., *with their chalybeate-alkaline waters*, enjoy as favorable a reputation in anæmic as Marienbad in plethoric corpulence. In Tarasp, finally, both kinds of healing springs are united—a highly desirable choice for two chief types of the disease, since a portion of the water has the character of simple alkaline *crenæ*, while another portion is chalybeate as well. The *Luciusquelle* is the principal representative of the first, the *Bonifaciusquelle* of the second species. A clear diagnosis of the type of the disease according to the general habit of the patient, and especially the physical signs of the circulatory apparatus, forms therefore an indispensable condition for the proper choice of a watering-place, as respects the spring, in each case of adiposity. It is not always sufficient to let a patient, who, by going repeatedly to *one* of the above-named watering-places, or by the use of *one* particular well, has found an essential alleviation of his sufferings, to run again next year in the old rut and try a new edition of the old "cure." The type of the disease changes as time goes by, and a case of anæmic corpulence may have developed itself from the plethoric form of the disease (see p. 671).

If it be thought that the weakening influence of a laxative Brunnen cure is, in all circumstances, to be feared in the case of a corpulent patient, or if there be other contraindications against the employment of this mineral water, a *hydriatic treatment* may with great advantage be substituted—that is to say, he may be advised to try the *cold-water cure* at a well-conducted establishment. Personally, we do not hesitate to adjudge to the hydriatic treatment at least the same amount of authentic value in the treatment of every form of corpulence as we give to the waters of Marienbad, Franzensbad, Tarasp, etc. ; and all the less because, with the internal and external employment of water, we may combine a regulation of the diet appropriate to the somatic conditions of the patient, and also the use of preparations of iron, when they are indicated by the presence of oligocythæmia. As to the mode in which these hydriatic proceedings act upon tissue-change and fat-production, we may refer to our remarks in connection with prophylaxis (p. 714). Through simple cold affusions or baths the general tissue-change is accelerated and the consumption of the stored-up fat in the production of heat increased, while the production of carbon is also increased; and the same thing takes place to a much greater extent, through more manifold and effectual methods of application of cold water, in the hydropathic cure. At the same time there is most probably also a more active new production of the red corpuscles, which, in a manner we have repeatedly described, acts as a hinderance to the tendency to further fat-production.

Since the *pneumatic* method of treatment has come more into favor, and in many places suitable cabinets have been erected for the breathing of compressed air, this physical agent has lately been warmly recommended for corpulence by some, and especially Sandahl.[1] We possess no individual observations concerning its action in the morbid condition of the organism, and cannot therefore confirm the favorable results of others from direct experience. These, however, decidedly call for further researches in the same direction, and deserve the attention of such physicians as desire to treat corpulence therapeutically, in a rational physiological manner; for, since we must suppose that under increased air-pressure there will be a corresponding increase in the weight of oxygen absorbed in each unit of the blood-plasma of the pulmonary blood, and that this increase will be stored up in the red blood-disks, we must also assume that, during each sitting, as a necessary temporary action of the pneumatic treatment, the hæmoglobin contained in these disks will also be more densely charged with oxygen. But on this denser charging depends the possibility of a brisker and more energetic oxidation-process in the whole region of the direct activity of the blood, and thus one condition is fulfilled which, under other circumstances favorable to the process of animal combustion, will, at any rate, prove itself rather favorable to a diminished than an increased tendency to fat-production.

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[1] Medicinskt Archiv atgivet af Lärare vid Carolinska Institutet i Stockholm. Vol. I. p. 1 et seq.

We finally mention, among the medicaments which have been employed in the direct contest with corpulence, and are still recommended by many, the preparations of *iodine*, and especially *mineral waters which contain it*—as, for instance, the Adelheidsquelle at Heilbronn (Jeitteles), *iodide of potassium* (Bright), *iodide of iron*, etc. The common tangle (*fucus vesiculosus*), extolled by Duchesne-Duparc with great emphasis as a true specific against morbid adiposity, also belongs to this category, the watery alcoholic extract prepared from this *alga*, given in doses of thirty grains three times daily, being said quickly to reduce the abnormal size of the body and weight of the patient (with increased diuresis), even in obstinate and severe cases of polysarkia. This proposed employment of iodine-containing drugs in corpulence is apparently based on the notion that iodine as an antiplastic drug will check the morbid development of fatty tissue, and even produce reabsorption of the already developed tissue. It therefore involves, properly speaking, a distinct theoretic conception of the pathological histology of the disease, since it presupposes not merely an increased distention with fat of the already formed, loose connective tissue (the fatty tissue), but evidently also a true proliferation (new cell-formation) of this tissue. Now, as this anatomical question, which we have been compelled repeatedly to touch upon in the progress of our discourse, is itself not yet finally settled, while the aforesaid pharmaco-dynamic character of iodine is likewise the theme of some controversy, we can at present only claim for the iodine treatment, strictly speaking, an empiric value and no rational character. At the same time the results which the observations of Bright, Duchesne-Duparc, and others, have given really seem to have in some degree justified the above theoretic conception, and further experiments with these drugs surely seem much to be desired. We also remember having seen repeatedly in non-febrile patients, who had been taking iodide of potassium constantly for a long time for certain other therapeutic ends, so great a reduction of their normal fat-padding, that we can by no means deny the possibility of a positively beneficial action of iodine in morbid polysarkia. Although, therefore, we have as yet no individual experience of the utility of preparations of iodine *specially in corpulence*, we should not hesitate a moment to employ them experimentally in serious cases of the disease, if the previously mentioned means of a different kind had left us in the lurch, and there were strong indications to procure the patient relief by any means whatever. Just as little, however, do we wish to bring the preparations of iodine, including the *fucus* recommended by Duchesne-Duparc, into new repute, or to propose them for use in all cases.

In many cases of corpulence, and especially such as are very far advanced, besides the essential treatment of the morbid condition itself, a *symptomatic* therapeusis for the warding off and removal of its most troublesome and dangerous phenomena claims a place. This has frequently, for instance, to devise remedies for the *hyperidrosis* of the patient, or in other cases for the troublesome *seborrhœa*, and in others again for the *intertrigonous* and *eczematous* inflammatory processes of the external skin in certain localities of the body mentioned before. The profuse sweating is, it is true, in a certain sense apparently a physiological corrective of the hinderance of the radiation of heat, and as such, strictly speaking, should not be the occasion of any treatment. It, however, constitutes a symptom which usually very painfully oppresses the patient, and is in reality excessive, inasmuch as the sweat-glands of corpulent individuals often apparently fall into a condition of pathological *hyperkrinia*, from too frequent physiological stimulation, and then, even when the body is at rest, or when the surrounding air is of moderate temperature, continue their immoderate secretion. As, besides, the hyperidrosis is a partial cause of the troublesome intertrigo and eczema, and also makes corpulent individuals particularly liable to diseases produced by cold (catarrhal and rheumatic affections), there is every reason for not allowing it to gain the upper hand too much. As means of checking this hyperidrosis, such general measures as cold ablutions, baths, and hydriatic procedures, or frequent washing of the surface of the body with water and vinegar (in the proportion of about 1 [of vinegar?] to 3), with decoction of sage and other slightly astringent lotions. In the higher degrees of *seborrhœa* the regular use of alcoholic and ethereal lotions proves most efficacious, less by diminishing the abnormal secretion itself than by dissolving and carrying off a portion of it. For *intertrigo*, when it is present, the ordinary sprinkling-powder of lycopodium or starch (*subtillissime pulverizatum*) may be used, and to this may fitly be added as an astringent a little oxide of zinc (in the proportion of 1 to 8); and for the sake of the perfume, a little benzoin, a very small quantity of oil of roses, or any other perfume. Finally, if serious eczema has occurred, the ordinary applications (astringent ointments, especially those containing preparations of lead, white precipitate, etc., or lotions of tannin, corrosive sublimate, etc.) may be employed. But, in advanced cases of corpulence, much more important than the treatment of skin-symptoms is *the contest with the symptoms of disorders of the circulation.* The more complete the development of a condition of permanent weakness of the heart in the patient, and the more manifest the development of *cyanosis* and *dropsical* symptoms, the more imperative grows the task of the physician to keep the heart's action itself properly regular as long as possible, by a general tonic treatment. He must, therefore, order the preparations of iron and a strong meat diet, and must carefully protect the patient from over-exertion of the heart, and let him as occasion requires have heart-tonics, such as digitalis. Where dropsy is present, this must be treated by exciting diuresis (by means of digitalis, squill, acetate of potash, boro-tartrate of potash, etc.), in order to diminish it; or by the occasional use of drastics, to get rid of it. In some cases of extreme corpulence with cardiac degeneration, where there was also great swelling of the liver and ascites unusually prevailed over the other dropsical symptoms, a combination of digitalis and calomel (morning and evening, a powder to be taken, composed of one and a half grains each of digitalis and calomel, and eight grains of white sugar) proved in our hands very efficacious as a diuretic and drastic prescription. The diaphoretic method so useful in most cases of dropsy seems less suitable as a hydragogue treatment where there is corpulence, because a further increase of the secretion of sweat in a patient who is already predisposed to sweating is certainly not advisable. That finally, in cases of necessity, we must sometimes proceed to evacuate the transuded fluid by puncture, requires no further discussion. Besides the dangers of chronic weakness of the heart and its consequences, corpulent patients are in danger of *acute attacks of insufficiency of the heart* and sudden general collapse. The treatment with respect to this must be chiefly prophylactic—that is to say, the patient must as much as possible be guaranteed against such attacks by the forbidding of violent bodily movements, and the withdrawal of causes of mental emotion; where this cannot be done, the ordinary powerful restoratives must be employed. Finally, we must not forget to pay proper attention to the most ordinary symptomatic indications, to see to the bowels, giving slight laxatives when constipation is present; to pay attention to the appetite and digestion of the patient, and to stir them up occasionally with suitable prescriptions (bitter aromatics, alkaline carbonates, preparations of rhubarb), when this seems necessary, etc., etc.

Concerning the special treatment of the particular *complications* of corpulence, we must refer the reader to the corresponding sections of this Cyclopædia. We must, however, at the conclusion of this chapter, again generally refer to *the greater malignity of intercurrent morbid processes, especially those of a febrile nature, in corpulent individuals.* This naturally requires, from *the therapeutic point of view, also particular attention*, and makes great foresight, as well as prudence, imperatively necessary in treating the complication, especially when it is of a febrile nature. The principal cause of the comparatively slight power of resistance manifested by the corpulent lies, as before mentioned, in *the laxity of their constitution*—that is, in the comparatively small power of physiological reproduction and restitution of their blood and other tissues of the body; frequently also (and, indeed, in all cases of anæmic corpulence), in the presence of true *oligocythæmia*, which latter may very easily proceed from habitual sluggishness of blood-production as a resulting phenomenon. It is now quite clear why, as a general rule, in corpulent persons who are seriously affected otherwise, it is necessary to avoid, as far as possible, all modes of treatment of a *weakening* nature, and why it is often decidedly dangerous to employ, in the treatment of the complications which occur, curative measures of which the principal or secondary effect will be the lessening of the vital substance of the body, and particularly of the red blood-corpuscles. Bleeding, even in the form of leeching, is, with patients who labor under inflammatory disease, under all circumstances a two-edged weapon, which much oftener does harm on the wrong side than good on the right side. The same holds good, though in a less degree, with *other depletory modes of treatment*—the continual use of *laxatives* and the *use of mercury* in cases in which, besides the intercurrent affection we have directly to treat, there is habitual corpulence present. All these therapeutic methods ought, as a rule, when the corpulence is rather of an anæmic character, always to be employed with great prudence, and never for any great length of time. The general principle in the treatment of every kind of intercurrent complication of adiposity must then be: that *everything is to be avoided that might easily completely destroy the constitution, already, without this, inclined to rapid exhaustion, and under the fresh load of the new complication.*

In opposition to this rather *negative and prohibitory* therapeutic principle frequently stands another just as important and more eminently *positive*, namely, that *when the complicating affection is itself of a debilitating nature, it should be deprived of this character as much as possible.* It is, therefore, manifest that the most radical indication is the *abortive* treatment of the complication. Where this is possible it is therefore indicated, not only for reasons of general utility, but with special reference to the already existing constitutional affection of which corpulence is the outward and visible sign. When, on the contrary, as is often the case, this abortive treatment is not possible, in treating the complication *those symptoms from which the danger of general exhaustion is most to be feared must be most energetically combated.* This latter indication is especially important where the complication is of a *febrile* nature; but at the same time it must be taken as an established fact that in febrile diseases the chief danger of exhaustion proceeds from *the fever itself*. *An energetic struggle with the febrile process*, by means of the most appropriate internal remedies (quinine, salicylic acid, digitalis) is, therefore, evidently the first task of therapeutics, and, moreover, often enough the only means of saving the lives of corpulent persons who are attacked by serious febrile diseases. *Neglect or insufficient exhibition of those internal antipyretics which are here specially required is*, *on the other hand*, *almost equivalent to the sacrifice of the patient.* We are finally persuaded that the much talked-of excessive mortality of the corpulent in febrile diseases might—not indeed altogether, but to a certain extent—be approximated to the ordinary level of febrile mortality, if the shyness of employing the appropriate antipyretics in such cases *in sufficiently large doses* were more generally overcome. These large doses, if the rules laid down by us in another part of this volume (see p. 454) be strictly adhered to, so far from putting the patient's life in danger by the production of serious collapse, are rather calculated continually to ward this off, since on each repetition, by transiently alleviating or interrupting the febrile process, they transiently paralyze the deleterious influence upon the function and nutrition of the heart and other vital organs, thus in many cases happily preserving the life of the patient until the spontaneous resolution of the complicating affection. That we should neither spare stimulants, nor from the beginning of the fever abstain from preserving the organic functions of the patient from total derangement, by a diet properly adapted to his real nutrition, is self-evident. At least it is so much so to ourselves, that we have here ventured expressly to refer to this point only because we have unfortunately seen this so important therapeutic duty neglected by others. If, in speaking of *the treatment of fever in corpulent individuals*, we have laid the chief emphasis upon a treatment by drugs as energetic as possible—by large doses of quinine (30 to 45 grains daily in *single* doses), or salicylic acid (70 to 90 grains in the same way[1]), or by the combination of one or other of these two drugs with digitalis, according to the method given on p. 447—and have said nothing so far about the *cold-water treatment* of the fever, we have done so not merely because this latter represents simply a symptomatic and not an essential treatment of the fever, but more particularly *because the hydriatic process, for reasons given already* (see p. 683), *has comparatively little cooling power in the case of fat persons.* But, since it is just in such cases that the danger of fever is particularly great, that the physician who trusts to cold water *alone*, in the treatment of febrile complications in corpulence, is evidently in a certain manner like a very imprudent general, who, while the enemy concentrates itself and attacks him in overwhelming force, dispenses with the best part of his own available strength, and with the weak remainder of his troops makes a hopeless resistance. This comparison is not extended to the proscribing the cold-water treatment altogether in such cases. On the contrary, this remonstrance is contained in it: *that we should at all times hold ourselves ready to combat the danger with all the means at our disposal*, and in fever, besides the treatment by drugs, should set energetically to work when possible with our hydriatic antipyretics, so as in some degree to obviate the disadvantages of the position.

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[1] On account of the many conflicting opinions respecting the antipyretic influence of salicylic acid which have recently been expressed, and of the statement which attri-

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butes to it dangerous caustic effects, we find ourselves here compelled to make the express declaration that the preparation used by *us* (procured from the Schweitzerhalle at Basle) acts powerfully and surely in the doses recorded, and that often employing it in the form of Limousin capsules, even after long-continued use, we have never found, in any case in which we had occasion to make a post-mortem examination, any caustic action whatever in stomach, intestines, etc.

SCROFULOSIS,

AND

AFFECTIONS OF THE LYMPHATIC GLANDS

IN GENERAL.

BIRCH-HIRSCHFELD.

LEEDS & WEST-RIDING
MEDICO-CHIRURGICAL SOCIETY

SCROFULOSIS AND AFFECTIONS OF THE LYMPHATIC GLANDS IN GENERAL.

Introductory Remarks.

THE pathological position of the lymphatic glands is determined mainly by two relations. The lymphatic glands must be considered as delicately porous filtering apparatuses, through which percolates the lymph flowing away from the tissues, while in certain regions the materials received by the internal surface of the body pass through the lymphatic glands. We find these glands, accordingly, most numerously developed where they correspond with organs which have the most intimate contact with the external world (lungs, alimentary canal).

By this relation we can understand the most intimate connection which exists between the diseases of the lymphatic glands and the morbid changes of the parts from which they receive their lymph. Just as we may with certainty discover the fine granules of coloring matter introduced into the skin for the purpose of tattooing, in the corresponding lymphatic glands, so we may be sure of finding molecular substances endowed with irritating properties, which in some manner entered the peripheral tissues, filtered off by the lymphatic glands, and acting there also as irritants. At present we are compelled to accept the theory that a considerable number of contagious and infectious processes are caused by such irritating molecular substances, and from this we can readily understand that wherever an infectious process is established in the periphery the corresponding lymphatic glands begin to swell, as a rule immediately—and most decidedly, too—whenever the infectious matter has penetrated more deeply into the tissues. It is only necessary to refer, in this respect, to the swellings of the lymphatic glands in erysipelas, diphtheritis, phlegmon, and numerous other infectious diseases.

We have, however, not always to deal with materials received from without. The lymphatic glands participate in other diseases of the region in which their afferent vessels have their radicles; any simple inflammatory process (as one created by mechanical causes) may carry from the tissues flooded with exuded constituents of the blood to the lymphatic glands materials which set up hyperplastic cell-proliferation in the latter. To a still greater degree the lymphatic glands are exposed to invasion by the elements of certain neoplasms. The quicker the rate at which proliferation takes place in a tumor, the greater the number of cells, and the looser the connection of the individual elements of the tumor between each other, the more easily will cells and cytoblasts of the tumor get into the interstices of the tissues, into the lymphatic vessels, and farther on into the lymphatic glands, there to undergo further development. Thus we recognize the infection of the corresponding lymphatic glands nearest to the seat of the primary tumor as an almost pathognomonic symptom of the malignant character of certain neoplasms, and, whenever these are beyond our means of immediate investigation, we lay the greatest stress on this circumstance.

It is easily seen from the above-mentioned relations that the diseases of lymphatic glands are essentially of a *sympathetic* character; but we have to remember, on the other hand, that these glands are the seats of lively physiological cell-formation, and that their structure is conformable to the type of a recent, as it were, unfinished tissue.

Now, if we recognize in certain constitutions a special anomaly in the reaction which the tissues show under irritating influences, we shall at once understand how such deviations manifest themselves principally in the lymphatic glands, and how, under such circumstances, irritants acting from the periphery may evolve important processes of disease in them. In such cases the affection of the lymphatic glands will assume the character of a certain independence, although originally it was not an idiopathic one.

Compared with the above-mentioned diseases of the lymphatic glands, the strictly idiopathic ones form only a small group, and in some of these even we may suppose that the affection of the glands only appears to be a primary one, simply because we do not yet know by what irritant the disease has been produced. If, therefore, we divide the diseases of lymphatic glands into three sections, it is self-evident that all *sympathetic affections of glands* must be classified with those pathological processes to which they owe their origin. In this respect the behavior of lymphatic glands, especially in infectious diseases, has already been accounted for in numerous passages of this work.

The second division has to be treated differently. We are accustomed to comprise under the name of *scrofulous affections* not only those affections of lymphatic glands which, although of secondary origin like the foregoing, acquire a *relative independence*, in consequence of a certain *predisposition of the tissues*, but also processes in other organs subject to the same constitutional influence. The affections of the lymphatic glands play so important a part in these, that, although only a partial phenomenon of the entire process, they have always been considered as the essential element of this process, and it has become a universal practice to treat of scrofulosis under the head of affections of the lymphatic glands.

Of the third group, finally, which comprises the *idiopathic affections* of lymphatic glands, some members have already been treated of, especially those which, separately or in connection with analogous changes in the remaining lymphatic tissues (spleen, bone-marrow), form the basis of *leukhæmia*. There remains, consequently, only a certain part of this group for special consideration ; and here we have to remember that we are treading on border-ground between the domains of Medicine and Surgery.

Literature.

Hippocrates, Lib. de glandulis. Cap. 3. Aphorism. III. 26.—*Galenus*, Comment. ad. aphor. Hipp. III. 16. Method. medendi. Lib. XIII. Cap. V.—*Celsus*, Opera, Lib. V. Cap. XVIII. § 11.—*H. Mercurialis*, De morbis puer. I. Cap. 5. § 11.—*Franc. Deleboe Sylvius*, Opera medica. Avenion. 1680. Praxeos med. Appendix. Tract. IV. § 51.—*Wharton*, Adenographia. Amstelod. 1659.—*Sauvages*, Nosologia methodica, Tom. III. p. 409.—*Faure*, *Bordeu*, *Charmetton*, *Majault*, *Goursaud* (Recueil des pièces qui ont concouru pour le prix de l'acad. roy. de Chirurgie. T. III. Paris, 1759).—*Renard*, Essai sur les écrouelles. Paris, 1769.—*Rich. Wisemann*, Several chirurgical treatises. Lib. IV.—*Robert Willan*, On the Kings-evil. Lond. 1746.—*Kuechler*, Diss. de glandulis puerorum. Lips. 1723.—*J. C. Ackermann*, De scrophularum natura. Lips. 1787.—*Hufeland*, Ueber die Natur, Erkenntniss und Heilart der Scrofelkrankheit. 1785.—*A. F. Hecker*, Libellus, quo morbum syphiliticum et scrophulosum unum eundemque esse evincere conatus est. Hal. 1787.—*Kortum*, Commentarius de vitio scrofuloso. Lemgoviae, 1789.—*Cullen*, First lines of the practice of physic. Edinb. 1796.—*Stoll*, Praelectiones in divers. morbos chronicos.—*Thomas White*, On scrofula and struma. 1780 (?). *Fr. Aug. Weber*, Von den Scrofeln, einer epidemischen Krankheit vieler Provinzen Europas. Salzburg, 1793.—*R. Hamilton*, Observations on scrofulous diseases. 1790 (?).—*Baumes*, Traité sur le vice scrofuleux et sur les maladies qui en proviennent. Paris, 1805.—*Stark*, Commentat. de scrofularum natura. Jenae, 1803.—*Carmichael*, *Henning* and *Goodlad*, On Scrofula, 1815 (?).—*W. Fare*, On the nature of scrofula. 1815 (?). *A. C. Baudelocque*, Monographie der Scrofelkrankheit, aus dem Franz. von *Martiny*. Weimar, 1836.—*C. G. T. Ruete*, Die Scrofelkrankheit, insbes. die scroph. Augenentzündung. Göttingen, 1838.—*Andr. Disse*, Die Scrofelkrankheit nach ihrem Wesen und einer darauf gegründeten Heilmethode. Berlin, 1840.—*G. W. Scharlau*, Die Scrophelkrankheit in allen Beziehungen zum menschlichen Organismus. Berlin, 1842.—*G. Négrier*, Die Behandlung der Scropheln, übersetzt von Kreutzwald. Bonn, 1844.—*Lugol*, Essays on the effects of iodine in scrofula. Translated from the French by W. B. O'Shaughnessy. London, 1831.—*P. Philipps*, Scrofula, its nature, its prevalence, etc. London, 1846.—*R. M. Glover*, On the pathology and treatment of scrofula. London, 1846.—*C. Holland*, The nature and cure of consumption, indigestion, scrofula. Lond. 1850.—*Lebert*, Lehrbuch der Scrophel- und Tuberkelkrankheit, bearbeitet von *Kochler*. Stuttgart, 1851.—*Duval*, Traité théorique et pratique de la maladie scrofuleuse. Paris, 1852.—*F. Balman*, Researches and observ. on scrofulous disease. London, 1852.—*R. Virchow*, Arch. f. path. Anat. 1847. Würzburger Verhandl. Bd. I. 1850. Bd. III. 1852.—Tuberculose und Scrophulose. Wien. med. Wochenschr. 1856. No. 24. Die krankhaften Geschwülste. II. Band. Berlin, 1864–1865. S. 582–607.—*H. Ancell*, A treatise on the constitutional origin of consumption and scrofula. London, 1852.—*E. Bazin*, Leçons théoriques et cli-

niques sur la scrofule. Paris, 1858.—*P. Price*, Scrophulous disease of the external lymphatic glands (Brit. med. Journal, 1860).—*Enrico Moretti*, Della natura della scrofola (Annal univ. di med. Vol. 169. p. 520).—*E. A. L. Huebener*, Pathologie und Therapie der Scropheln. Wien, 1860.—*Hérard et Cornil*, De la phthisie dans ses rapports avec la scrofule. Union méd. No. 124. 1866.—*Billroth*, Scrophulosis, *Pitha-Billroth*, Handbuch der Chirurgie. I. Band. 2. Abth. —*J. Paget*, On senile scrofula. St. Barthol. Hospital Rep. III. p. 412.—*O. Schueppel*, Untersuchungen über Lymphdrüsentuberculose und die damit verwandten und verwechselten Drüsenkrankheiten. Tübingen, 1871.—*C. Friedlaender*, Ueber die Beziehungen zwischen Lupus, Scrophulose und Tuberkulose. Centralb. f. d. med. Wissensch. 1872. N. 43.—*C. Hueter*, Die Scrophulose und ihre locale Behandlung als Prophylaxe gegenüber der Tuberkulose. 1872.—*Volkmann's* Samml. klin. Vorträge. No. 49.—*W. Moxon*, On the nature of scrofula and its relation to tubercle. Med. Times and Gaz. Dec. 1873.—*Wright Treves*, On the condition of the circulation in scrofula. Lancet. 1873. p. 568. —*C. Friedlaender*, Ueber locale Tuberculose. *Volkmann's* Samml. klin. Vortr. No. 64.—*The same*, Untersuchungen über Lupus. Virch. Arch. LX. 15.—*G. Bizzozero*, Ueber die Tuberculose der Haut. Centralbl. f. d. med. Wissensch. 1873. No. 19.—*Koester*, Ueber locale Tuberculose. Centralbl. f. d. med. Wissensch. 1873. No. 58.—*Haward*, On scrofula. St. George's Hosp. Rep. V. p. 99.—*E. Nagel*, Ueber Frühformen der Scrophulose (Wien. med. Presse, 1873. No. 28–30).—In this connection may be mentioned the treatise of *E. Rindfleisch*, on chronic and acute tuberculosis, and that of *H. Ruehle*, on pulmonary consumption and acute miliary tuberculosis, in volume V. of this Cyclopædia. In the list of works enumerated at the beginning of the chapter on Pulmonary Consumption will be found the titles of the treatises published by the following authors: *Morton*, *Baillie*, *Portal*, *Bayle*, *Laënnec*, *Andral*, *Cruveilhier*, *Villemin*, *Hoffmann*, *Buhl*, *Waldenburg*, *Klebs*, and others.

Historical Remarks.

The history of Scrofulosis cannot be separated from that of tuberculosis. In surveying the development of pathological ideas, we find that at certain periods tuberculosis comprises only a part of the territory of scrofulosis, while at others the term tuberculosis becomes the general one to which scrofulosis subordinates itself as a relatively unimportant subdivision.

Although it seemed at different times as if pathologists had succeeded in drawing a distinct dividing line between tuberculosis and scrofulosis, the barriers were broken through again soon after being established. Just at the present time their territories overlap each other to such an extent that the question may again be raised whether a separation of scrofulosis from tuberculosis be justified. Under such circumstances it seems necessary to institute a somewhat more detailed investigation into the historical development of these theories, because in this way the best basis may be found for a definition of scrofulosis. A review of this kind is moreover also of great interest, because it shows the coincidence of some of the most recent theories with very ancient views.

The term scrofulosis is connected with the tumefaction of the lymphatic glands of the neck, which even to-day is looked upon as a very characteristic element of this affection. The "χοιϱαδες" of Hippocrates was translated into the Latin "scrofulæ," although it is true the older Roman authors made use of the term "struma" for these tumors. It was intended to give prominence to the similarity presented by the thickened neck, the diminished prominence of the chin, and the swelled upper lip—all consequences of the swelling of the glands—with the physiognomy of the hog. It is less probable that this term was selected, because glandular tumors also occur not unfrequently in the hog.[1] That the ancients were acquainted with scrofulous affections of the glands as obstinate forms of disease frequently occurring in young subjects, may be proved from the works of Hippocrates, Celsus, and others.

The term "tubercle," in the specific sense in which it is used by modern authors, cannot be found in the works of ancient writers, as Virchow has satisfactorily demonstrated. It is used by these exclusively in its morphological meaning. Neither does the Greek term φυμα, which is often translated with "tubercle," correspond with the meaning which is given to it to-day, else it might be maintained that Hippocrates already placed the scrofulous tumors of the glands by the side of the tuberculous ones, "χοιϱαδες και τἀλλα φυματα." The term φυμα is principally used for accumulations of pus, especially for cold abscess.

The tubercle was at all events unknown to Hippocrates. Pulmonary phthisis was considered as a disease caused by suppuration of the lung.

Mediæval authors, who in the main followed the teachings of the ancients, were equally unacquainted with the tubercle, and could not therefore attempt to refer to it the existence of scrofulosis. In the sixteenth and seventeenth centuries, however, the rising study of anatomy and the more frequent autopsies led to better acquaintance with the post-mortem appearances of pulmonary phthisis, and then began also the comparison of the tubercles found in the lungs with scrofulous lymphatic glands. In this way Sylvius was led to the hypothesis of the normal existence in the lungs and other organs of exceedingly minute glands, invisible in their physiological or healthy condition, which, a certain predisposition being given, grow larger, suppurate, and give rise to phthisis. This hypothesis, that pulmonary tubercles are formations analogous to scrofulous lymphatic glands, remained prevalent for a long time. Wharton calls tubercles of the lungs "glandulæ adventitiæ morbosæ;" Morgagni recognizes the similarity; Morton imagines scrofulous phthisis to be the most frequent form of pulmonary consumption, and explains it by the choking-up of a certain gland-like part of the lung. A reaction against the identification of the two processes began with the discovery of miliary tubercles. Stark, and especially Reid, opposed the view that invisible glands occurred normally in the lungs. Cullen, on the other side, who refers the origin of scrofulosis to a specific scrofulous poison (acrimonia scrofulosa), lays stress on the apparent identity of the matter expectorated from ulcerated pulmonary tubercles in a very great number of cases with that by which scrofulosis is caused.

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[1] See *Kortum*, l. c. I. page 33.

When, towards the end of the eighteenth century, scrofulosis became the subject of a lively discussion, stimulated by the prize problems of diverse medical associations, authors still moved within the sphere of these theories. An essential progress is, however, observed in another direction. The ancients saw the essence of scrofulosis in the glandular tumors, although recognizing their origin on a constitutional basis. (Hippocrates, for example, and Galenus, in similar manner, refers scrofulosis to a pituitous and cold condition of the humors.) The knowledge, however, that this disease not only manifests itself in the glandular tumors, but also shows itself in certain peculiarities of the general habit of the body, and makes itself felt during the progress of morbid processes in the skin, mucous membranes, and bones—this knowledge appears with distinctness for the first time in works of the past century, especially in those of Cullen (where we already find the accurate description of the scrofulous habit, usually attributed to Hufeland), of Stoll, Ackermann, Kortum, Hufeland, Bordeu, and others. Pathologists of that period went even so far in this respect as to connect the most heterogeneous morbid processes, as scabies, fevers, rachitis, and parasitical tumors like cysticerci (hydatids), with scrofulosis.

The views generally held at that period on this question may be summed up in the sentence that scrofulosis reigned supreme over the domain of tuberculosis, tubercular phthisis itself being looked upon as a scrofulous disease. This hypothesis of the intimate connection between scrofulosis and pulmonary phthisis was even not dropped after the investigations of Stark and those of Reid had rendered doubtful the correctness of the hypothesis of Sylvius.

Kortum expressed his opinion in reference to this connection (an opinion which, by the by, closely resembles the theory taught in the most recent time on the relations of tuberculosis and scrofulosis) in the following characteristic sentence: "It is sufficient that experience should have amply established the fact that the lungs of scrofulous subjects are frequently attacked by tubercles; that these tubercles have their seat not only in the bronchial glands, but in all parts of the lungs, and that tubercular phthisis is most frequently of scrofulous origin."

Even Baillie, who had recognized the origin of ordinary pulmonary tubercles from miliary tubercles, did not distinguish them from scrofulæ; they appeared to him as "metastatic scrofulæ." Bayle, and after him Laënnec, whose labors heralded a new epoch, were the first to give a totally altered relative position to scrofulosis and tuberculosis, although on closer inspection the difference established by these authors will be found to confine itself essentially to the nomenclature. While formerly, as we have just shown, scrofulous disease of the glands formed the starting-point from which the explanation of pulmonary tuberculosis was attempted, lung-tubercle now formed the basis. As the essence of tubercle was not thought to lie so much in its form as in the cheesy substance which characterizes it in a certain period of its existence, pathologists were inclined to classify all processes, in which cheesy substance is formed, with tuberculosis, and scrofulous glands were considered, according to this view, only as a small subdivision of tubercular disease. Laënnec himself, it must be admitted, laid much stress on the development of the cheesy substance from an originally gray material, while his successors simply contented themselves with the cheese, indifferent as to the manner in which it had originated.

Those affections which heretofore were classified under the head of Scrofulosis, but did not fit into the new scheme, were set off as processes of simple chronic inflammation.

Scrofulosis, formerly deemed so important, and discussed from so many different aspects, fell now into greater and greater discredit as the doctrines of Laënnec were gradually digested and assimilated by physicians, and for some time men who still clung to the older ideas about it were regarded as wanting in scientific character and lagging behind the progress of the day. There was indeed no want of opposition to Laënnec's doctrine, and some of its opponents (Andral, Broussais) gave prominence to the fact that the cheesy substance did not exclusively arise from tubercles, and might develop from the products of inflammatory processes; but still scrofulosis remained a mere chapter of tuberculosis, because all minds were laboring under the idea that the conception of scrofulosis was completely covered by that of tuberculosis. We have only to mention in this connection the names of Velpeau, Rokitansky, Cruveilhier, Vogel, whose views coincided on this point, however much they diverged in other directions.

The opposition against this identification of scrofulosis with tuberculosis proceeded mainly from those men who were forced by clinical experience to the conviction that scrofulosis had after all meant something else besides cheesy glandular tumors. In this respect we have to name especially Lebert, who in his influential treatise advocated the view that an independent position must be conceded to scrofulosis by the side of tuberculosis. It must be remembered, however, that Lebert thought he had found a specific element of tuberculous products in the well-known "tubercle-corpuscles;" and as he was bound to find these corpuscles, the products of shrivelled-up cells, in all possible cheesy products, he was led by his experiences to separate the cheesy glandular tumors from scrofulosis, and to classify them with tuberculosis. Lebert consequently characterizes scrofulosis as a disease which localizes itself principally in the skin, the subcutaneous connective tissue, the organs of special sense, the joints and bones, and appears in the form of various chronic inflammations inclined in an eminent degree to suppuration and ulceration; while the lymphatic glands of scrofulous subjects become mainly the seat of tuberculosis.

In Germany Lebert's doctrine of specific tubercle-elements could not gain ground from the beginning. Very soon after its promulgation Reinhard came forward with the proof that the so-called tubercle-corpuscles can be produced from shrivelled-up pus-cells.

It was reserved to the acute logic of Virchow to spread light on the entangled aspects of this subject as of many others, and up to the most recent time the domain of scrofulosis seemed so well divided off from that of tuberculosis that a relapse into the former condition of confusion was not to be expected. This was true, however, only in regard to Germany. In France the example of Virchow was followed only by a few authors (Cornil and Hérard among others). Virchow demonstrated simultaneously with Reinhard that the cheesy substance does not arise out of a specific primary condition, but is the product of a regressive metamorphosis (necrobiosis), which may occur in the most heterogeneous tissues. "Tubercle," on the other hand is, according to his view, an originally descriptive expression which it is best to restrict to miliary neoplasms, the product of heteroplastic luxuriance of tissues, which product is, however, inclined to cheesy metamorphosis in consequence of its want of blood-vessels and the liability of its elements to decay. A cheesy product was accordingly to be accepted as tuberculous only after sufficient evidence had been given of its origin from miliary tubercle. On the strength of these propositions Virchow opposed the identification of scrofulosis and tuberculosis. He went even farther, and distinguished with the greatest precision the cheesy glandular tumor from tuberculosis, saying with emphasis that all who do not classify these tumors with scrofulosis, exclude just its most characteristic product. The changes in the scrofulous lymphatic glands are at first essentially of a *hyperplastic* nature (hyperplastic lymphoma), but the cells are from the beginning badly constructed, and consequently very soon lapse into cheesy degeneration. Other processes, accompanied by cheesy degeneration which hitherto had been classed with tuberculosis, were considered as scrofulous by Virchow, the cheesy masses being in his opinion nothing but inflammatory products metamorphosed under the influence of a peculiar constitution. The pulmonary disease which since Laënnec went under the designation of tubercular infiltration, was accordingly termed by Virchow scrofulous broncho-pneumonia. For all that, and notwithstanding the closeness with which Virchow distinguishes scrofulosis from tuberculosis, he admits the existence of an internal connection between the two processes, and keeps himself open to the possibility of considering tubercles as a kind of heteroplastic scrofula.

There was indeed no want of numerous pathologico-anatomical facts to prove the intimate connection between scrofulosis and tuberculosis, as regards their etiology, and experimental pathology soon began to tell in this direction.

Dittrich already referred tuberculosis to the reception by the blood of products of retrogressive metamorphosis. Buhl,[1] standing on the basis of pathologico-anatomical experience, expressed himself still more definitely in the proposition that tuberculosis is caused by accumulations of cheesy materials of inflammatory origin. No other disease, however, so frequently leading to the formation of cheesy masses as scrofulosis, the frequent termination of scrofulosis in tuberculosis appeared totally clear, given the correctness of the premise stated above.

A full description of the several experiments that have been made in regard to this infection would involve us in too many details, and we shall therefore content ourselves with only a few references to them.

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[1] Zeitschrift f. rat. Med. 1857.

Villemin, and especially Klebs, arrived at the result that it is not every cheesy substance, nor any casual irritating influence, no matter of what nature, which causes tuberculosis, but that this disease is one of infection, which, like syphilis, spreads through the agency of a specific virus. It became accordingly necessary to class even scrofulous glandular tumors with tuberculosis, as positive results had been obtained by the inoculation with matter from cheesy lymphatic glands of scrofulous subjects.

Most authors, however, who occupied themselves with experiments on these questions, arrived at different results. Cohnheim and Fraenkel, Wilson, Fox, Waldenburg, and others, all advocated the opinion that tubercles might be generated in animals (especially in rabbits, which are prone to the formation of cheesy products), by operative interference of the most varied description; but their opinions diverged on the question whether or not the connecting link of an inflammatory product in the state of cheesy degeneration were a necessary condition of this result. It is easily understood how this view would keep its adherents from contradicting the doctrines of Virchow; they could without difficulty grant the hyperplastic nature of scrofulosis, and comprehend, nevertheless, why it led so frequently to a tuberculous termination.

A new turn of this question is based on the more accurate histological study of tubercle, on the strength of which the results of experiments were subjected to a revision which led to doubts whether these experiments were so convincing in their results as they had hitherto been universally considered.

The investigations of E. Wagner[1] prepared the ground for a more accurate knowledge of the minute structure of tubercle, and these were followed immediately by the researches of Schueppel, so important especially to our subject. The most important result of these researches consisted in a more accurate definition of the characteristics of tubercle as compared with simple inflammatory neoplasm, and in the demonstration of its occurrence in products which so far had been counted among those of inflammatory or simply hyperplastic processes. The claim now raised by Schueppel, of a tuberculous character for scrofulous disease of the lymphatic glands, is founded on a thoroughly different method of demonstration from the one followed previously and especially by Lebert. Schueppel accepts the criterion of tubercular disease insisted on by Virchow in its whole breadth; he is far, however, from identifying cheesy transformation with tuberculosis, and declares that only after actual demonstration of the preliminary stage of the cheesy nodule, viz.: the gray miliary tubercle, may tuberculosis of the lymphatic glands be assumed with certainty. This demonstration has been furnished by Schueppel's numerous and searching investigations to such an extent that no further doubt is left as to the frequent occurrence of well characterized tubercles in the lymphatic glands, partly in the form of secondary development with pre-existing tubercles of other organs, partly, however, as primary tuberculosis, to which latter category belong those very conditions which have been regarded heretofore as the most characteristic products of scrofulous disease. It must here be observed, however, that Schueppel does not deny the occurrence of simple hyperplastic processes in the lymphatic glands of scrofulous subjects; on the contrary, he gives prominence to the opinion that such hyperplastic processes may precede the development of tubercles. The cheesy degenerations, on the other hand, so frequently occurring in the scrofulous, he identifies with tuberculosis, and goes even so far as to look upon the cheesy degeneration of pure, non-tuberculous lymphomata as yet to be demonstrated. His experience then leads him to the standpoint of Klebs, with whom he coincides in the supposition that only certain kinds of cheesy material contain tubercular virus, such only as arose from the disintegration of tubercles.

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[1] Arch. der Heilkunde. 1870.

We have to remark, moreover, that Schueppel does not consider primary tuberculosis of the glands as an idiopathic disease, its only primary element being tuberculosis—its cause, however, an irritation conducted to the gland from the periphery. On the other hand, he presupposes a special condition which might be termed *tuberculous diathesis*, in order to explain the various reactions against this irritation in different individuals, and even in the several organs of the same body. The essence of scrofulosis is to be found in the increased vulnerability of the parts, and, inasmuch as predisposition to tuberculosis always means predisposition to inflammation, scrofulosis is identical with the tuberculous diathesis.

In many respects related to these views are those of Rindfleisch, which shall not be given here in detail, because they have been already stated in another part of this work.[1] We only draw the attention of the reader to his opinion that those forms of inflammation which run a specific course in scrofulous constitutions, produce a virus which, received into the humors of the body, gives rise to tuberculosis. Although a primary inflammation of this kind need not absolutely contain an anatomical element which could be claimed as tubercle, Rindfleisch designates such inflammation already as primary tuberculosis, because it gives rise to secondary tuberculosis of the lymphatic glands, and defines the tubercle of a scrofulous subject as a circumscribed focus of scrofulous inflammation.

The domain of tuberculosis was still further extended by other investigations which belong to the most recent period. We first mention Friedlaender, who, in all deep-seated scrofulous affections of the skin and bones, found, as a rule, copious eruptions of tubercular nodules, and, therefore, arrives at the conclusion: "All the more important scrofulous affections are intimately associated with the formation of tubercles." Not only in the foci of scrofulous affections, however, but also in processes of an entirely different nature miliary tubercles were proved to exist by Friedlaender, as, for instance, in a superficial ulceration of the cervix uteri, in old ulcers, in the stroma of cancer, in lupus. On the other hand, Friedlaender maintains that tubercles artificially produced in animals do not correspond in structure with the genuine tubercle of the human subject, from the absence of the characteristic signs (giant-cells, epithelioidal cells). Friedlaender denies, therefore, the validity of the proof adduced from experiments on animals in the decision of questions connected with tuberculosis. Koester, who had demonstrated the occurrence of tubercles in the granulations of fungous arthritis prior to Friedlaender, found afterwards miliary tubercles in caries, ostitis, and osteo-myelitis, as well as, almost without exception, in cheesy lymphatic glands ; he saw them also in chronic pericarditis and pleurisy, in a primary syphilitic sore, in elephantiasis of the labia majora, etc. He does not, however, like Friedlaender, take the appearance of tuberculous matter to be the primary element, at least in scrofulous affections, but declares emphatically that in all these cases tubercles appear, not in healthy tissue, but only in proliferating connective tissue and granulations, the result of inflammation or neoplastic growth.

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[1] Vol. V.

The discovery by E. Wagner, Rindfleisch, Buhl, and others, of the almost constant occurrence of tubercles in cheesy pneumonia, that results in pulmonary phthisis, may be mentioned without going into details ; and finally, Buhl's assertion, that tubercles may be found in every extensive growth of newly formed embryonic connective tissue, deserves a general reference.

The essential result of this historical survey may be briefly stated in the following sentences :

Originally, the term scrofulosis was confined to cheesy tumors of the lymphatic glands. Later on, a number of inflammatory processes, especially in the skin and bones, were added, and the whole of the phenomena explained by a constitutional alteration of the organism ; still later, phthisis pulmonalis was counted in with scrofulous affections.

After the discovery of miliary tubercles, when cheesy deposits in the lungs were ascribed to miliary or infiltrated tuberculosis, this genetical view was applied to other cheesy products, especially to scrofulæ of the lymphatic glands, and scrofulosis became merged in tuberculosis.

When the origin of cheesy substance from non-tuberculous processes, especially of an inflammatory nature, was proved, the designation tuberculous was limited to nodulated, non-vascular, heteroplastic formations ; most of the processes, hitherto counted among the scrofulous ones, were regarded as simply hyperplastic or inflammatory, the products of which tended to cheesy degeneration in consequence of some constitutional liability to disintegration.

An intimate etiological connection between scrofulosis and tuberculosis was again recognized when experiments had confirmed the theory that tuberculosis is caused by the absorption of inflammatory products in the state of cheesy degeneration, or at least regressive metamorphosis.

When, in the most recent time, the occurrence of tubercle in most deeper-seated scrofulous affections was demonstrated histologically, the view, that scrofulosis mainly depended on the appearance of tuberculous inflammations (local tuberculosis), began to gain new ground.

Pathogenesis and Etiology.

It is self-evident that a discussion of the constitutional and external causes of scrofulosis is not possible until the meaning of this term has been clearly defined. On the other hand, it is not less evident, from what has been stated above, that the main difficulty of the definition of scrofulosis consists in fixing the line which divides it from tuberculosis; consequently, the question of the pathological position of tuberculosis, especially in its connection with inflammation, cannot very well be avoided altogether. We are obliged, therefore, to give special reasons for our general pathological view of these relations before we can enter into the special features of the pathogenesis and etiology of our disease. What has already been said about the frequent occurrence of tubercles speaks in favor of the doctrine advocated by many old and recent authors, according to which the most intimate connection exists between tuberculosis and inflammation. This connection is regarded from different points of view, and the main question at issue is whether or not a specific character must be attributed to the primary inflammation which leads to tuberculosis. This question must be answered in the affirmative by those who look upon tuberculosis as originating in a virus transmitted to the body in some manner, and therefore regard it as an infectious disease. This view necessarily leads to another, already adopted by the advocates of the former, that scrofulosis is actually an effect of the tuberculous virus.

With the accumulation of instances of the occurrence of well-characterized tubercles in processes of irritation, produced by the most different infectious and non-infectious causes, it became, however, more and more difficult to maintain the opinion that the primary process which leads to tuberculosis is started by a specific virus.

Taking this for granted there still remains open the question whether it be not necessary to presuppose a special local or general *predisposition* for the development of tuberculosis from irritative processes of various origin, and whether the constitution which we designate as scrofulous be not involved in this very question. It cannot be denied that in a very large number of cases this opinion holds good, and, as we have mentioned before, that already at a very early period unprejudiced observation led to the proposition—that scrofulosis furnishes the soil on which pulmonary tuberculosis is developed.

If all the conditions, however, are considered under which tubercles are formed, the opinion that a *specific constitution* cannot be regarded as the general basis of tuberculosis, obtrudes itself irresistibly.

Virchow has drawn attention to several facts in illustration of this. He relates among others the case of a man, eighty years of age, who was attacked by tubercular pericarditis, but had never suffered from scrofulous affections. Whoever has frequent opportunity for anatomical investigation of chronic pericarditis with exudation, will rarely meet with a case in which he does not succeed in demonstrating tubercles in the newly formed tissue, and very often these are cases of purely local tuberculosis. The same may be said of chronic pleurisy, and even of many cases of tubercular pneumonia. It is frequently impossible to find anything pointing to pre-existing scrofulosis, either in the history of the case or by the most searching post-mortem investigation. Whoever would insist on designating such subjects as scrofulous for the sake of his theory would have to do so just because they became tuberculous. It is true that cheesy products are found in the affected organs, at least in the majority of cases of this description, and it might seem justifiable to claim for these cases a "scrofulous inflammation," out of which arose local tuberculosis, if we accepted the opinion that the occurrence of cheesy degeneration in any place is already sufficient for designating the process as a scrofulous one. In this way, however, the term scrofulosis becomes *one of general anatomy*, is used for a definite species of metamorphosis, and loses its former pathological meaning, at least until it can be demonstrated that every instance of cheesy degeneration occurring in the body is based on a certain constitutional anomaly. As long as it is universally conceded that purely local conditions may become causes of cheesy degeneration, and that all circumstances may lead to it which impede the removal of inflammatory products, abounding in cells, from the tissues at a period of insufficient nutrition, we would oppose the practice of calling every case of cheesy pneumonia scrofulous, or of talking, in conformity with ancient use, of gonorrhœal scrofula. One might just as well term syphilitic gummata, which frequently are given to cheesy degeneration, syphilitic scrofula, or create a species of scrofulous cancer; the term scrofulous would, in short, have to be taken in as vague a sense as the word "diphtheritic" at the present time.

We cannot, therefore, admit that either cheesy degeneration or tuberculosis develops exclusively on the basis of a special constitutional anomaly, viz., Scrofulosis.

Speaking without prejudice and in conformity with facts, we must declare that *the development of the neoplasm called tubercle is connected with inflammations of a definite course.*

If the characteristics of such inflammations are inquired after, they may be described as those forms of exudative inflammation in which the removal of the products of inflammation is impeded or prevented.

This prevention may be caused by various circumstances. In the first place, the condition of the exudation itself must be taken into account. It is evident that exudations abounding in cells will of themselves furnish less favorable conditions for absorption than those mainly consisting of watery elements. Then, as Virchow has especially pointed out, there may be inherent to the exuded cells a certain liability to decay (as we can see not only in single individuals, but in entire classes of animals); and here we have to deal with a constitutional factor to which we shall have to recur on account of its great importance to our subject. In addition, even purely local conditions may be the cause of defective absorption (disturbances of circulation, plugging up of veins and lymphatic vessels, deposits in the parenchyma of organs).

We have here to consider another relation which, it is true, has not been completely cleared up. Although the theory of inflammation is still an unsettled question, it must nevertheless be granted, in view of the sagacious experiments of Cohnheim,[1] that an *alteration of the walls of the blood-vessels,* obscure as it may be thus far in a morphological respect, is of essential importance as to the character of the inflammatory exudation. The greater this disturbance, the larger is the number of cells in the exudation. On the other hand, the cessation of the exudation depends on the restoration of the physiological integrity of the walls of the vessels; if this is incomplete the emigration of the corpuscular elements of the blood continues, although to a diminished degree. If to this is added an insufficient activity of the channels of absorption, then all the conditions are given for the retention of the exudations and the starting of regressive metamorphosis. The origin of a chronic inflammation from an acute beginning is best referred to an imperfect repair of the altered walls of the vessels, but for an *a priori* chronic exudative inflammation we have to presuppose either the action of a weaker irritant, which, however, reproduces itself continually, or a condition of the vascular walls which especially disposes them to a lasting alteration (increased vulnerability with diminished recuperative power); or, finally, a constitution of the blood (respectively the circulation) might be thought of, which makes it unfit for the restoration of healthy action in the disturbed vascular walls.

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[1] Neue Untersuchungen über die Entzündung. Berlin, 1873.

The condition of the vascular walls determines not only the character of the exudation, but also the formation of new tissue, another process frequently connected with inflammation. The vascularization of the cellular products of inflammation is, as shown more and more clearly by recent investigations, affected by the agency of the vascular apparatus itself, which agency is in turn influenced by the textile constitution of the vascular wall, on the one hand, and the actual conditions of the vascular contents (lateral pressure) on the other. We need not go into details to prove that a deeply and permanently affected vascular apparatus will not act efficiently in this respect also, especially when a mechanical impediment is furnished by an accumulation of crowded exudation-cells in the tissues. That such a state of things will equally lead to insufficient nutrition of the inflamed parts, and a predisposition to the occurrence of regressive metamorphosis, will also be understood without further demonstration.

By these remarks we mean only to suggest how various the conditions (partly of a local and partly of a constitutional nature) are which determine the chronic process of inflammation and the tendency which it shows to form regressive products.

If we now inquire into the connection of tuberculosis with inflammations proceeding in this manner, we have to confess that a clear insight into this relation is not yet possible. The almost constant coincidence of tubercular eruption and cheesy products in parts so inflamed prompted the supposition of a virus being formed in the regressively changed products of inflammation which gave rise to a specific neoplasm, the tubercle. The experiments on animals speak especially in favor of this view, and clinical observation also leads to the hypothesis of an infectious matter formed in the body itself. Especially in regard to scrofulosis physicians could at no time rid themselves of the idea that the agency of a specific acrimonious humor or scrofulous virus was essential to its production.

The supposition of such a hypothetical virus is, however, by no means inevitable.

When the above-mentioned conditions lead to a peculiar necrobiosis of a portion of the inflammatory products, which we call cheesy degeneration, we find in another contiguous portion of the cells a somewhat imperfect attempt at the formation of new tissue, a process frequently even preceding the cheesy degeneration. Division of nuclei, formation of new elements take place; in many cases the process is arrested after the multiplication of nuclei; the cell increases in volume, but no differentiation of the cell-protoplasma resulting in new individual cells ensues (in this manner the formation of giant-cells may be imagined); but all these proceedings show an ephemeral character from the start, vascularization is wanting, and the cells soon lapse into regressive metamorphosis in spite of their attempt at neoplasia in the beginning. It is probable *a priori* that the cells nearest to the vessels would most likely present a tendency to such progressive changes.

It may furthermore be well supposed that the cytoblasts and descendants of such cells of impaired vitality may get into the blood and lymph currents, and put forth the same weak efforts in remote parts. The possibility of metastatic formation does certainly not necessitate the supposition of a specific tubercular virus, just as little as in the case of carcinoma, sarcoma, etc. This view of the nature of the neoplasm called "tubercle" might, however, be very well combined with the hypothesis of a specific virus formed in the regressively changed products of inflammation.

According to the hypothesis, the outlines of which are given above, *tubercle might be regarded as a degenerated species of inflammatory neoplasm* (*granulation*), *determined by necrobiotic processes.* This hypothesis, which agrees very well with observed facts and renders the connection between chronic inflammation and tuberculosis somewhat better understood, would not have been discussed here in detail if it had not recently received a substantial foundation by the important experiments of Ziegler.[1]

This interpretation of the connection between tuberculosis and inflammation, which in its essence only amounts to a more definite expression of the opinions published long ago by others, has been discussed in a more detailed manner, and on the basis of an inquiry into the results of recent investigations on tuberculosis, by the author.[2] This circumstance is mentioned because the concurrence of the views at which Ziegler and the author arrived by different methods, speaks for the correctness of the interpretation alluded to.

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[1] Centralbl. f. d. med. Wissensch. Nos. 51 and 58. 1874.

[2] Deutsche Zeitschr. f. pract. Med. 1874. No. 5.

Ziegler introduced beneath the skin, periosteum, and into natural cavities of dogs and rabbits thin disks of glass, cemented together in such a manner that fine interstices were left between the disks, into which the white blood-corpuscles could migrate from the surrounding parts. If the disks were left *in situ* for a longer period of time, the cells accumulated between them underwent regressive changes in most cases; in others, however, progressive changes took place, either development of vascularized connective tissue, or formation of a reticulated tissue with epithelioid cells imbedded therein, and rich development of giant-cells; in fact, products which exactly correspond to the structure of what E. Wagner and Schueppel recognized as reticulated tubercle. On the strength of these observations Ziegler lays down the proposition: "Tubercle with its giant-cells is a focus of inflammation in which the colorless blood-corpuscles accumulating at any point undergo a peculiar development. This development is, in my opinion, dependent on defective cell development, unequal to the task of forming new connective tissue, nature being obliged to stop short at the mere attempt to form it."

In the light of this interpretation the relation of tuberculosis to inflammation in general, and the position of scrofulosis in particular, becomes clear and intelligible. If the general proposition, that the inflammations occurring in scrofulous subjects have no specific character, is received without dissent, it has nevertheless been also conceded that the scrofulous constitution is characterized by the tendency to inflammation in consequence of comparatively slight irritations and the persistent nature of the inflammatory disturbances (increased vulnerability and diminished recuperative power). One can easily understand now how, under these circumstances, tubercles arise so frequently. If, on the other hand, such a course of inflammation is by no means exclusively dependent on a scrofulous constitution, if it may occur also under different local and general conditions, it is clear without further demonstration that tuberculosis may arise without scrofulosis, although in the scrofulous subject we find especially favorable conditions for the development of tubercles.

Another point regarding this connection, however, deserves our special attention. Although the origin of tuberculosis from a decidedly inflammatory process may be demonstrated in many cases, there are facts also favoring the supposition that sometimes primary tuberculosis may occur without any preceding inflammation, that is to say, in like manner as secondary tubercular eruptions. And here the transmission of tubercular elements, capable of development, from one organism to the other, or, if that should be preferred, the infection by ready-made tubercular virus, may come into play.

If, according to what has been said above, the development of tubercles in inflammations of the scrofulous must not be considered as something accidental, as a mere complication, if it is even demonstrated by facts that the more severe disorders (especially of the lymphatic glands) affecting scrofulous subjects proceed with the formation of tubercles in almost all cases, we might assert—with all deference to the proposition, that tuberculosis is almost always preceded by a process of irritation—that the most essential of the symptoms which grouped together form the idea of scrofulosis belong to tuberculosis, and that the whole course of scrofulous inflammation with the persistent character of its products is dependent on the tubercular process itself. Those who look upon the tubercle as the primary element in all the more severe affections ascribed to scrofulosis, will, of course, be still more prone to merge scrofulosis in tuberculosis. We hold with Koester that in the majority of cases, the development of tubercles takes place secondarily, but the appearance of tuberculosis is regarded as the main characteristic of scrofulous inflammation with so much truth that in this process we may recognize at once the essential element. Should any one attempt—as Lebert has done, on the ground of different premises, however—to separate local tuberculosis from scrofulosis, he would, in the language of Virchow, throw aside just the classical product of scrofulosis. We are of opinion that it is best not to make such a separation. Holding on to the internal relationship of inflammation and tuberculosis, we arrive at the natural conclusion that under the clinical term of scrofulosis are comprehended inflammations of a chronic and tuberculous nature, which develop themselves on the soil of a constitutional predisposition. The essential condition for the retention of the conception scrofulosis is the constitutional basis on which both of these processes develop themselves one out of the other. By regarding this constitutional anomaly as a tubercular diathesis no real progress is attained, as in a great many cases of scrofulosis the development of tubercles remains local. In these cases only a local diathesis could be thought of, while, on the other hand, the abnormal vulnerability of the parts manifests itself by inflammatory processes in the most different organs; in this respect the term tuberculous diathesis would be too narrow. In the next place, as we have already explained, the tubercular diathesis may also originate from disturbances which have nothing in common with scrofulosis, and in this respect the tuberculous diathesis would occupy a wider ground. For clinical reasons also it is advisable to retain scrofulosis. Practitioners have at all times opposed the attempt to get rid of this nosological conception, and, indeed, whoever has had some experience in the diseases of childhood, must acknowledge that the manner in which certain individuals react against noxious influences leads to the assumption of a definite constitutional habit. Whether the term lymphatic constitution or inflammatory diathesis be employed, or the old designation scrofulosis be retained, makes of itself no difference as to practical purposes, for we are accustomed to use the old names for most diseases, although the original meaning of these terms does not any more agree with the modern conceptions thereof.

Having premised these general remarks, we may try to give a short definition of scrofulosis. Leaning on previous definitions, especially those furnished by Virchow and Billroth, we may designate *scrofulosis as a constitutional anomaly which shows itself by changes partly of an inflammatory, partly of a hyperplastic nature, excited in the tissues by a comparatively slight noxious influence,—changes which are endowed with insufficient recuperative power, and are therefore prone to lapse into regressive metamorphosis and, following thereupon, into local tuberculosis.*

As noxious external influences most easily affect the surface of the body (skin and mucous membrane), the primary seat of scrofulous inflammations is mostly found on this, while morbid processes are set up in the lymphatic glands by the lymph conveyed to them from it. Scrofulosis consequently shows its effects, as a rule, first in the integuments and the lymphatic apparatus.

If we inquire further into the *nature* of those constitutional changes, we find a great number of hypotheses at our disposal, and the great variety of the explanations given leads us of itself to the conclusion that so far nothing definite can be said on this subject. From the earliest time an abnormal constitution of the lymphatic apparatus has been suspected, because the affections of the lymphatic glands were always regarded as a very important element of the disease. Some assumed too great a consistency of the lymph; others, the formation of an acrimonious matter in the lymph; others again ascribed the disease to excessive formation of lymph, while some authors (Bell, Hufeland, and others) thought that they had discovered the essence of the disease in the weakness or atonic character of the lymphatic system. According to individual views of authors on general pathology, deficient innervation (Holland), abnormal constitution of the blood, weakness of circulation, etc., were called in to aid an explanation.

Attempts to trace scrofulosis back to a specific virus were not wanting even in the earliest times.

The manifold analogies which are presented by the course and manner of propagation of scrofulous affections with some forms of syphilis especially led to such views, although all previous attempts at experimental demonstrations of a scrofulous virus had failed (Kortum and others). Repeatedly there arose the notion that an infection nearly allied to syphilis was at the bottom of scrofulosis, that the latter was in fact, as it were, a degenerated form of syphilis. The similarity of certain products of hereditary and acquired lues venerea to the substance found in glands affected with scrofulosis would make this view probable, and the cases of congenital scrofulous nodes described in former times by different authors were no doubt syphilitic gummata. The opinion that scrofulosis must be traced back to hereditary syphilis was already opposed by Kortum, and may be now considered as discarded. It must be remembered, however, that a certain internal connection between syphilis and scrofula must after all be admitted.

There is nothing striking in the fact that parents suffering from venereal cachexia generate scrofulous children, and not more surprising is the fact that syphilis, when it attacks a scrofulous subject, assumes a specially severe and obstinate form, particularly in the lymphatic glands and the osseous system.

In more recent times several authors returned to the view that scrofulosis is caused by a specific infectious matter, a view resulting from the identification of scrofulosis and tuberculosis, together with the belief in the existence of a specific tubercular virus. That we are opposed to this view is shown by our having advocated above the opinion, which recognizes the tubercle as a special form of inflammatory neoplasm, and thereby divests it of every specific character.

Moretto (l. c.) had already suspected that scrofulous diseases are caused by low organisms, and Hueter, who in general ascribes a pathological importance of the farthest bearing to the monads, makes these organisms play an essential part in the genesis of scrofulosis also.

Hueter finds the essential element of the scrofulous constitution in the *dilatation of the lymphatic vessels by the relatively great quantity of the alimentary juice occurring normally in the period of childhood.* These vessels extending to and ramifying in the superficial layers of the skin and mucous membranes, these integuments lose that firmness of texture which protects them against the invasion of inflammation-producing organisms suspended in the air.

The monads having entered, at first produce the primary scrofulous affections of the skin and mucous membrane, and, proceeding further on in the direction of the lymph current, cause the affections of the lymphatic glands. In aid of this hypothesis Hueter lays down the assertion that the cheesy matter is mainly made up of monads, an assertion which he fails to prove sufficiently by his detailed description.

In the present state of our knowledge it will generally be best to stand by the propositions enunciated by Virchow on the nature of the scrofulous constitution, as no safe basis has been found as yet which would enable us to go beyond this somewhat unreliable foundation. Virchow ascribes scrofulosis to *a certain weakness or incompleteness in the structure of the lymphatic glandular apparatus*, which weakness will manifest itself all the more in the yet growing unfinished glands of the juvenile organism. For the dependence of weakness of certain systems and organs on a *hereditary predisposition* we have numerous proofs in other chapters of pathology.

We may here only mention hæmophilia (hemorrhagic diathesis), another hereditary disease which must be absolutely attributed to a special weakness in the structure of the circulatory apparatus, although so far it has not been possible, as little as in regard to scrofulosis, to find anatomical proof of that imperfect structure.

We would, however, be justified in assuming a hereditary specific vulnerability of the blood-vessels, in the case of scrofulosis, besides the imperfect character of the lymphatic apparatus. As already mentioned above, such an assumption would make the progress of inflammation in scrofulous subjects more easily understood. Symptomatic phenomena, moreover, are not wanting which speak in favor of a certain weakness as well as of an abnormal irritability in the circulatory apparatus of scrofulous subjects. In this respect we have to mention dilatation of the subcutaneous veins, abnormally strong reaction of the cutaneous vessels, especially in the so-called erethic form of scrofulosis, great changeableness in the frequency and character of the pulse.

It is difficult to decide whether a certain misproportion between the liquid and solid constituents of the body play an important part in the origin of this disease, as Rindfleisch[1] supposes. Clinical experience, however, does not give the impression that anæmia always precedes the appearance of scrofulous disease.

Our knowledge of the anatomical and physiological conditions which constitute the basis of scrofulosis being still defective, we must confess that the causes which give rise to the abnormal constitution are by no means clearly made out. As in many other diseases the etiology of which is yet obscure, numerous influences of great variety are accused as the originators of this one.

As one of the most important causes, which, as indicated above, is very probable *a priori*, according to our ideas on the nature of scrofulosis, and materially supported by the facts of experience, must be recognized *hereditary transmission*. The number of cases by which this relation may be illustrated is indeed not great enough to establish a direct proof by the statistical method, but we are nevertheless justified in pointing out the unanimous opinion of those physicians who commanded a larger practical experience as to the occurrence of scrofulosis. Two circumstances are of special importance in this respect. In the first place, it can frequently be shown that the parents of scrofulous children were also scrofulous in their early age, and, in the second place, parents affected with tuberculosis generate frequently scrofulous children, the latter circumstance, however, being by no means the rule.

Every practitioner has frequent opportunities for observing how children of parents affected with pulmonary tuberculosis grow up apparently healthy, never in their childhood presenting any symptoms of scrofulosis, but still becoming subject to tuberculosis at the time of puberty. In view of the frequency of such observations it must be admitted that hereditary transmission of the predisposition to pulmonary tuberculosis may take place without the mediation of scrofulosis. Such are probably cases of hereditary transmission of weakness in the respiratory apparatus itself, which may coexist with a normal condition of the lymphatic apparatus. On the other hand, scrofulosis is hereditary in some families in which the occurrence of tuberculosis is very rare.

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[1] See Vol. V. of this Cyclopædia.

The question, so much discussed formerly, whether the predisposition only to scrofulosis could be transmitted or the disease itself inherited, must be looked upon as settled, the decision being given universally in favor of the transmission of the mere predisposition, because there is no foundation in fact for the other alternative.

Lebert was able to prove hereditary transmission in one-third of eighty-eight cases. Balman ascertained that among 141 scrofulous patients nine had lost the father, and eleven the mother by tuberculosis, while thirty cases of tuberculosis had occurred in near or distant relatives of the rest.

It is also supposed that, independently of the hereditary transmission of scrofulosis properly so-called, *old age*, *near blood-relationship*, and a *cachectic condition* of the parents may become causes of a hereditary predisposition to this disease. Probable as this supposition may be, there is as yet no statistical confirmation of it.

The *geographical distribution* of scrofulosis is so universal that there is hardly a single locality which may be said to be free from it. On the other hand, we cannot point out any climatic peculiarities of those countries or parts of countries in which scrofulosis occurs as a prominent endemic disease. We find it in the cold northern region and in the temperate zone among all the civilized nations of Europe, as under the tropics (among Negroes, Hottentots, etc.). It has been stated by travellers that in some regions (according to Livingstone, for example, in some regions of Central Africa, according to others among the Indians and Kabyles) scrofulosis is almost unknown. This immunity, if it should be confirmed, would have to be ascribed to a certain

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[1] Compare the detailed account of it in *A. Hirsch's* Handbook of Pathological History and Geography. I. 494–521.

mode of living rather than to climatic influences. It might, perhaps, be admitted that countries in which sudden changes of temperature occur frequently, exert a special influence because such changes furnish a potent exciting cause of scrofulosis. In this regard the statement is of interest that persons, especially children, transplanted from the tropics to the temperate zone, are frequently attacked by scrofulosis.[1]

How widely scrofulosis is spread in some countries, we may gather, for example, from the statement of Philipps, according to whose estimates twenty-four per cent. of the whole population of England are suffering from scrofulosis; in France the average of conscripts declared to be unfit for military duty on account of scrofulosis amounted to one per cent. in a period of twenty years,[2] while an examination of the French captives in the late Franco-German war furnished sufficient evidence that scrofulosis occurs with extraordinary frequency even among the soldiers of the French army.

The estimates of the frequency of scrofulosis, from tables of mortality, are very unreliable, because in most reports rachitis and scrofulosis are not distinguished, and again cases of death from diseases of joints and bones, a large proportion of which originate from scrofulosis, are not counted under this head; besides that, it is highly probable that in the case of scrofulosis, the rates of sickness and mortality are not parallel, because social conditions exert an undeniable influence on the course and severity of this disease. According to our present information on this subject the average rate of mortality from scrofulosis is from 6 to 16 in 1,000 deaths from all causes.

The conditions of the *soil* do not seem to exert any influence on the frequency of scrofulosis; this must be said especially of its elevation, which, according to some authors, considerably influences the occurrence of tuberculosis. Scrofulosis occurs with equal frequency in the low plains of Holland, on the plateau of Castile, in the mountain villages of Saxony, Silesia, and Bohemia, 2,000–3,000 feet above the sea-level; and, according to MacClellan, in the Himalaya Mountains even in sites 13,000 feet high. The humidity of the soil is equally devoid of any constant relation to the frequency of our disease, as will be seen from the fact that some authors maintain a relation of reciprocal exclusion between malaria and scrofulosis, while others look upon swampy soil as an element favorable to the development of scrofulosis. Of the geological formation of the soil the same may be said, so far as we know at present.

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[1] *Cooper*, Annual Med. Rev. II. 130. *Pearson*, ibid. 42.

[2] *Boudin*, Traité de géogr. et de statist. med. II. 1857. From the data given on page 699 of this work, it may be inferred of how little importance the character of the climate and soil (elevation and other conditions) really is as to the frequency of scrofulosis. Corsica, the Mediterranean coast, and the northern department of Pas-de-Calais furnished the smallest number of scrofulous subjects; the department of Bas-Rhin, Rhine, Seine, Moselle, Puy de Dôme, Hautes-Alpes an equal number; while contiguous departments frequently presented opposite extremes of frequency.

The connection between the frequency of scrofulosis and the *social conditions* of a given population is universally admitted, and rests on very good proof, although it is not possible to point out individual circumstances as the essential ones, because we have to deal with a concurrence of causes, the influence of every single one of which cannot be accurately defined.

In all probability poverty favors the frequency of scrofulosis, as a general rule.[1] This relation is not a constant one; there are regions in which the greatest misery prevails while scrofulosis rarely occurs there,[2] and on the other hand it may be frequently found in thrifty districts, just as daily experience proves the existence of it among families in the most affluent circumstances. The probable cause of this phenomenon is to be found in the circumstance that in poorer districts a great many weak children die in the earliest period of life which might have been saved by proper care, and furnished a large increase of the scrofulous population as elsewhere. On the other hand, it must not be forgotten that the *quality of food* is of great importance, and improper diet is as frequent in rich districts as among poor populations.[1] The custom of bringing up children by the spoon prevails almost universally in some rich agricultural districts, and experience teaches us moreover that excess may have the same effect as want.

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[1] *Marc d'Espine* states that in Geneva eight per mille of the deaths among the well-to-do-classes are caused by scrofulosis, while among the total population sixteen per mille occur from the same cause. It must be remembered, however, that the death-rate does not accurately express the rate of sickness.

[2] *Virchow*, Arch. f. path. Anat. II. p. 170, 1848, found a district in Upper Silesia, in which typhus prevailed along with the highest degree of social misery, remarkably free from scrofulosis.

The diet of children in the first period of life has from time immemorial been regarded as an important element in the etiology of scrofulosis.

The general proposition that a spoon-fed child shows less resistance against morbific influences than one nursed at the breast, is not difficult to understand, but this is also the sum of our knowledge on this subject.

Certain articles of food have been held responsible for the disease, for instance, potatoes and rye bread in excessive quantities, and a coarse vegetable diet in general. Those authors who looked upon diseases of the alimentary canal as the primary cause of scrofulosis (Carmichael, Hufeland, and others), were especially inclined to attribute great influence to this agent, which appeared all the more important because definite indications could be deduced from this connection for dietetic treatment. Hufeland certainly goes too far in saying that every child could be made scrofulous, especially by improper diet; but the influence of diet cannot be denied altogether.

There is good reason for looking upon a coarse vegetable diet as hurtful in this respect, because it implies the consumption of relatively large quantities of food deficient in really nutritious substances, and, besides that, mechanical irritation of the intestinal mucous membrane from the very nature of the materials of this class. When introduced into the alimentary canal of a new-born child, adapted to an exclusive milk diet, the irritating effects of such improper food will show themselves all the more severe. Besides the mechanical irritation, we have to consider that caused by decomposing and rotten ingesta of this description.

Admitting the influence of bad food, and understanding without difficulty how catarrhal irritation of the intestinal mucous membrane and inflammatory cell proliferation in the lymphatic apparatus of the alimentary canal may arise in this manner, one can see in all this mainly an *exciting cause*, which favors the appearance of scrofulosis only on the ground of an existing predisposition. In this respect bad food is to be placed among the noxious irritating influences which generally cause scrofulous affections in the skin and mucous membranes.

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[1] We mention here only the statement of *Huss* that scrofulosis is very frequent in Schonen, the richest province of Sweden, where infants, almost immediately after their birth, are fed on coffee, sour bread, and potatoes. A similar state of affairs is found in thrifty districts of Bavaria, Saxony, etc.

A second factor which has been represented as one of the fundamental causes of scrofulosis already by Kaempf, and later by Baudelocque, is *bad air*. Here we have again to deal with a condition to which the poor population of large cities is especially liable, where many families are crowded together in small apartments with insufficient ventilation and exposed to the influence of vitiated air in an eminent degree. If this condition really exerted the influence ascribed to it by Baudelocque, we would be obliged to assume a striking contrast in the frequency of scrofulosis among the urban and rural populations; this contrast, however, does not exist in reality.

Philipps has already proved that the facts stated by Baudelocque are incorrect, especially in regard to England, where scrofulosis is actually more frequent in the rural districts than in the large towns. Lebert mentions, among other districts, the cantons of Vaud and Geneva, celebrated for their pure atmosphere, where scrofulosis is found as frequent among the rural population as in the towns. In the ore-mountains of Saxony also scrofulosis is very frequent, as Ettmueller states (and the author is able to confirm from personal observation).

In spite of all this it cannot be denied that vitiated air exerts a favorable influence on the development of scrofulosis. That children living in the country spend more time in the open air, is very true, generally speaking; but, on the other hand, it must be admitted that the dwellings, and especially the sleeping apartments, are much more unhealthy in the rural districts than in towns. The accumulation of animal and human excreta in the vicinity of dwellings, the disinclination of the rural population to ventilate their rooms sufficiently, the faulty construction and overcrowding of school-rooms in most places, all this sufficiently proves that children living in the country are by no means exempt from the evils of bad air. In instituting such comparisons it would, moreover, be necessary to go much further into details; that the occupation is of great importance (domestic industry or agriculture) in this regard, is self-evident.

The great influence exerted by vitiated air is especially demonstrated by the great frequency of scrofulosis in places of confinement, where, in many cases, the diet is perfectly healthy.

Hirsch (l. c.) mentions a large number of facts in illustration of this. Autenrieth[1] drew attention to the frequency of scrofulosis in penitentiaries (so-called *penitentiary-scrophulæ*). Of special interest is the statement of Doepp that in a boarding-school at St. Petersburg four times as many girls as boys were affected with scrofulosis, although their diet and room accommodations were the same; the cause of this difference was found in the persisting sedentary habits of the female pupils and their greater confinement to the small rooms of the institution.

The author has before him the sick lists of the Saxon Blind Asylum, mainly inhabited by children, for a period of thirty years. The greater part of these children were already affected with scrofulosis at the time of their admission into the institution. From these tables it appears that the cases of scrofulosis have decreased to less than one-half of the previous number (from twenty-five to ten per cent. of all cases of sickness), since the pupils have been required to take frequent exercise, especially gymnastic exercises, in the open air.

Besides the above-mentioned causes, great stress has been laid on *deficient culture of the skin.* The influence of this factor has, however, been certainly overrated; scrofulosis being frequently found in persons of cleanly habits, while populations covered with filth may remain comparatively free from it (scrofulosis is frequent in England and Holland, rare in Palermo, for example).

The influence of improper food on the origin of scrofulosis has been already mentioned, but only as one of general hurtfulness. Lately the suspicion has been raised that, through the means of food, and especially of *cow's milk*, a specific matter may be transmitted which gives rise to disorders corresponding in their progress to certain forms of scrofula.

It was pointed out first by Villemin, and then by Klebs, that the symptoms of animals artificially infected with tubercular matter corresponded with those of scrofulosis, but so far no proof was furnished that this analogy could be considered as an etiological identity, and no such origin as in the case of inoculated animals could be asserted for the scrofulosis of children. When, however, the pearl disease of cattle was recognized as a disease equivalent to tuberculosis, and when, later on, it had been demonstrated that this disorder could be transmitted not only by inoculation but also through the milk, the opinion could be maintained that cow's milk might become a vehicle of infection, and its use threaten danger to young children.

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[1] Spec. Nosologie und Therapie. Würzburg, 1836. II. p. 333.

It is not possible to enter here into the details of this highly important question. We have only room for a few remarks. In the first place, we shall give prominence to the histological identity of the pearly nodules of cattle with human tubercle, which is now established beyond doubt.

The suspicion as to the identity of "pearl disease" with tuberculosis was already expressed in earlier times. The apparent reasons against this identity, drawn from the investigations of Virchow, who compared the minute structure of the pearly nodule with that of some species of lymphosarcoma, fell to the ground, since, by the investigations of E. Wagner, the structure of human tubercle has become more accurately known, and Schueppel[1] demonstrated the complete correspondence in the structure of pearly nodules and tubercles.

Of still greater importance to our question are the positive results obtained by feeding different species of animals (hogs, calves, rabbits) on the milk of cows affected with pearl disease. We call attention in this respect to the experiments of Gerlach, Zürn, Harms, Klebs, Chauveau, and others,[2] from which it may be seen that tuberculosis may be generated most easily in herbivorous, but also frequently in omnivorous animals by feeding them on such milk. And, what is of the greatest interest to our subject, in some cases of tuberculosis so communicated, the affection of the lymphatic glands is the most prominent change. The analogy with some forms of human scrofulosis and tabes mesenterica becomes all the more striking, as not only the mesenteric but also the cervical glands become tuberculous.

On the ground of such facts, Bollinger expresses the opinion that certain forms of scrofulosis are nothing else but manifestations of tuberculosis in its incipient stage, and accepts the view of Villemin, who concluded from his experiments (according to the positive or negative result of his inoculations) that there is a specifically tubercular and a non-tubercular scrofulosis.

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[1] Ueber die Identität der Tuberculose und Perlsucht. Virch. Arch. 1872.

[2] See *Bollinger's* article on Tuberculosis by Inoculation and Feeding. Arch. f. exp. Pharmac. und Pathol. Vol. I. Nos. 4 and 5. 1873.

The pearl disease being a very frequent disorder among cows, especially in the vicinity of large cities (according to Gerlach, more than fifty per cent. of the live stock in Hanover are subject to this disease; according to Guenther and Harms, only one-third of one per cent.; according to Zürn, in the vicinity of Jena, from sixteen to twenty per cent.; while Bollinger estimates the rate of sickness at three per cent. at the utmost), there is no lack of opportunities for infection, if we suppose that man is, like other omnivorous animals, susceptible to the virus transmitted in the milk.

To draw definite conclusions from the results of the above-mentioned experiments, for the purposes of human pathology, would, as yet, be hazardous. Aside from the possible sources of error which may arise from the circumstance that the animals selected for the experiment—pigs especially—are frequently subject to cheesy degeneration of the glands, searching crucial experiments are still wanting; and, first of all, the question has to be settled, whether a specifically tubercular substance is absolutely indispensable for the production of positive results.

The author believes that this question deserves special attention, because he found that in rabbits, fed on catarrhal sputa, or even on common pus, cheesy affections of the mesenteric glands were produced in several cases. Before admitting the analogy of these glandular tumors with those found in the scrofulosis of man, it would, therefore, be necessary to institute more accurate microscopical investigations, which are wanting thus far in the above-mentioned experiments.

Finally, great stress must be laid on the circumstance that so far not a single fact has been made known which would go to prove the infection of human subjects by the milk of cows suffering from pearl disease. The question deserves, however, to be kept before the profession, and it would be specially interesting to collect data of comparative statistics in reference to the ratio of cases of human scrofulosis and pearl disease occurring in certain regions.

According to what has been stated above, hereditary predisposition plays the most important part in the etiology of scrofulosis, while, on the other side, unfavorable hygienic conditions, especially those in regard to food and air, excite this disease, or at least favor the development of its seeds, existing from the time of birth. Thus we find here already an intermingling of *predisposing* and *exciting causes*. In the latter respect, however, a great number of other agents come into play, all irritative processes in fact, the anomalous constitution of scrofulous subjects, as we have already remarked, being characterized by a peculiar inflammatory reaction of the tissues against irritants of relatively even insignificant importance. A noxious influence, which, in a healthy child, generates only a slight transitory cold, a mild conjunctivitis, causes, in a scrofulous one, an obstinate chronic coryza, a conjunctivitis of chronic duration, which may proceed to the severest forms of keratitis, etc.

Setting aside traumatic and mechanical irritations, certain infectious diseases must be accused, before all others, of exciting the breaking out of scrofulosis. Very frequently the first symptoms of the disease appear immediately after an attack of *measles*. As this disorder causes considerable irritation not only of the skin, but also of the mucous membrane of the eyes and the respiratory tract, the connection of cause and effect is easily understood.

Scarlatina, diphtheritis, typhoid fever, small-pox, and whooping-cough are among the less frequent exciting causes.

Frequent experience shows that *vaccination* also may not infrequently be followed by a breaking out of scrofulous symptoms. In such cases it is difficult to convince the non-medical public that this may happen without the transmission of any infecting matter through the instrumentality of the vaccine virus, a circumstance successfully made use of by the agitators against vaccination.

It is to be supposed that, in the majority of these cases, vaccination only excites the dormant disease, for it is frequently possible to find in the previous history of the vaccinated child, or in the condition of its parents, brothers, and sisters, sufficient reasons for a pre-existing disposition to scrofulosis. Whether it be possible to transmit scrofulosis, respectively tuberculosis, by lymph taken from a scrofulous child, cannot be asserted with any degree of certainty either in the positive or in the negative. The experiments on animals, which seem to speak in favor of such an assertion, are to be judged of with the greatest reserve, because, even granting that tubercles may be transmitted by inoculation, the question always recurs, are these tubercles the product of an infecting material introduced from without, or merely the result of inflammatory irritation on the basis of a constitutional predisposition? At all events, the caution of the imperial (German) statute on vaccination, which prohibits the taking of lymph from a scrofulous child for the purpose of vaccinating others with it, seems justified; this caution, however, becomes illusory, in the majority of cases, so far as first vaccinations are concerned, because scrofulosis generally does not show itself during the first years of life, and proof for the possible existence of a scrofulous constitution can be found only by an examination of the physical condition of the parents, brothers, and sisters of the child.

However frequently we may succeed in finding a definite irritation as exciting cause for the breaking out of scrofulosis, there are, nevertheless, cases enough in which the disease has apparently a spontaneous origin. Balman, for example, could point out an exciting cause only in one-half of his cases; but we must not infer from such statements that there really was none at all. The primary occurrence of scrofulosis in portions of the skin and mucous membrane which are exposed to frequent irritation, speaks of itself for the influence of an irritant which may be so insignificant, however, that it is overlooked.

If, in conclusion, we look to special individual conditions related to the frequency of scrofulosis we find that *sex* exerts no essential influence in this respect. Some authors assert greater frequency of scrofulosis in the female, others, on the contrary, in the male sex. It appears well ascertained, however, that the severe forms of the disease, ending in death, especially those accompanied with affections of the bones and joints, occur with somewhat greater frequency among boys.

The assertion that scrofulosis lasts not rarely beyond the age of puberty in the female sex, while in the male it dies out at that period, is not unfounded in fact. This difference has been explained by the peculiar physiological character of the female organization, which even in adult life resembles more closely that of the child.

Dolaeus remarks already that scrofulous tumors of the glands are more frequent among adult females than among men, and sees in that fact a divine punishment of female vanity which delights in hanging all sorts of jewelry around the neck.

As to *age*, scrofulosis occurs with greatest frequency between the third and fifteenth years. Glandular tumors especially occur seldom before the second year, while cutaneous eruptions, otitis, etc., are not unfrequently observed much earlier in children who afterwards became affected with scrofulous tumors of the glands.

It is very rare that scrofulosis makes its first appearance in adult life after puberty; more frequently the disease continues from early life beyond that period; sometimes we observe the appearance of symptoms, answering the description of scrofulosis, at an advanced age in people who had been scrofulous in their childhood. Thus, we have occasion now and then to see a new accession of spondylitis in old people who, when young, became subject to kyphosis in consequence of cheesy ostitis, the disease having remained stationary for a long period of time.

Of all cases of scrofulous glandular tumors observed by Lebert one-twelfth occurred during the first five years, one-fifth between five and ten years, almost one-third between ten and fifteen, and two-sevenths between ten and twenty.

Different attempts have been made to refer the predisposition to scrofulosis to certain peculiarities of bodily habit. It was asserted that light-haired children, with blue eyes and delicate skin, incline to scrofulosis, an assertion which has been refuted by the extensive statistical researches of Philipps, which conclusively show that the different conditions of skin and hair stand in the same relation to each other among the scrofulous as among the respective populations in general.

Whatever else has been said of the scrofulous habit will be referred to in another chapter.

The connection between *rachitis*, *cretinism*, *favus*, and scrofulosis which was formerly believed to exist, may be dismissed very briefly. While formerly all these disorders were comprised under one head, and even scabies added thereto, we can now assert very definitely that there is no connection between them whatsoever (except that favus might act as an exciting cause), and that no one of these diseases either induces or excludes the appearance of the others.

Pathology.

General Course of the Disease.

Since the cause of scrofulosis has been found in a general disturbance of nutrition, many authors have endeavored to detect certain peculiarities in the habit of the body from which the dormant predisposition to this disease might be recognized even before the appearance of its symptoms. Accordingly, we find already in the writings of Cullen, Stoll, and especially of Hufeland, Kortum, and others, detailed descriptions of the *scrofulous habit.*

Just as a torpid and an erethic form of phthisis were assumed, so two principal types of the scrofulous habit were created.

The habit of *erethic scrofulosis* is characterized by a delicate frame of body, deficient muscular development, fine skin inclined to blushing, transparency of blue interlacing veins, especially in the temporal region and on the eyelids, soft hair of mostly light color, beautiful blue lustrous eyes with dilated pupils, lively irritable temper, early development of the sexual desire and of the intellect.

Duval goes so far in this respect as to assert that all persons distinguished by prevalent development of the brain and greater intelligence, owe their superiority to the fact of having been somewhat scrofulous in their childhood!

Some authors insist, moreover, on the peculiar irritability of the mucous membranes, especially that of the respiratory tract in the erethic form of scrofulosis, which consequently furnishes the largest number of cases of pulmonary phthisis.

The habit of *torpid scrofulosis* is characterized by a burly frame of body, bloated appearance, richly developed adipose tissue (vulgarly called flabby flesh), and muscles incapable of great exertion. The head is large, the physiognomy becomes heavy and unpleasant by the thick nose and upper lip, the broad jaws and short, thick neck; a tumid abdomen completes the physical features of this habit, while the psychological character is distinguished by a sluggish phlegmatic disposition and deficient intellectual development.

Among scrofulous patients, some are no doubt to be found who represent the image of both these extreme types in a salient manner; the impartial observer will, however, concede that the majority of cases lie between the two extremes, or represent a mixture of the characters of both, as it happens with all such classifications.

How imperfectly the ground was covered with this classification may be readily seen from the fact that it was considered necessary to assume a so-called "medium" habit, standing between the erethic and torpid one (Ruete). In this way it could not be difficult to place each individual case under a distinct general head. How imperfectly those succeed who want to point out characteristic signs of the scrofulous habit already before the appearance of any symptoms of scrofulous disease, may be best seen by reading such descriptions as Bazin's, who characterizes the said habit in such a manner that every imaginable kind of whatsoever constitutional peculiarity is comprised by it.

Some features claimed as characteristic of the scrofulous habit really belong to the already developed disease.

Among these are the thick upper lip and nose, the bloated appearance of the face, and the tumefied neck. Very often physiognomies, previously in no way striking, are seen to undergo these characteristic changes after tumefaction of the cervical glands (and consequent arrest of the lymphatic and venous current) has taken place. This physiognomy is, however, wanting in all those cases in which the main seat of scrofulosis is in other parts—for example, in scrofulosis of the mesenteric glands; here other phenomena appear in the foreground—tumid abdomen, great emaciation, anæmia, etc.

What remains, after deducting the changes wrought by the fully developed disease, is by no means characteristic of scrofulosis, and designates nothing but extreme constitutional types, as we generally find them during the period of childhood.

We must, before all, remember that the conditions under which the development of scrofulosis most frequently takes place, are most apt to impress on the respective individuals a morbid appearance. If bad air, insufficient or improper food, and descent from weak parents, exert an influence on the development of this disease, we shall easily understand why children become scrofulous who were previously anæmic and poorly nourished. That such phenomena, however, and scrofulosis do not stand necessarily in the relation of cause and effect, that we are not justified in ascribing scrofula to "lymphatic anæmia," as has been done, is readily shown by the simple fact that children in the best social conditions, of blooming aspect and apparently luxuriant health, become not infrequently the victims of scrofulosis.

After all that has been said, we have to look for the chief criterion of the scrofulous constitution in the abnormal reaction of the body against irritating influences. We may grant, however, that it is not unimportant, in a therapeutical as in a prognostic point of view, to lay stress on the general habit of scrofulous patients. In this respect even the extremes of erethic and torpid scrofulæ may be retained, provided always that we do not mean thereby something specifically characteristic of scrofulosis.

The course of scrofulous affections is an eminently varied one. It is therefore almost impossible to give a general description of it. We shall understand this difficulty all the more readily because we know that we have to deal, not with specific products of a scrofulous infection, but with a modification of different morbid processes by a constitution of peculiar predisposition.

In many cases, as we have stated already under the head of Etiology, a definite exciting cause may be recognized, with which the breaking-out of the scrofulous affection is connected, as, for instance, vaccination, measles, etc. In other cases the exciting cause is extraordinarily slight (catarrhal conjunctivitis, mechanical injuries, caries of a tooth, etc.). Finally, in a large number of observed cases, it is impossible to find out the least cause, and here we have probably to deal with cases in which the disease develops itself on the basis of a very strong hereditary predisposition.

We have no means of determining what symptoms appear first when the exciting cause begins to produce its effects ; we do not know why in one case the disease principally affects the skin and mucous membrane, while in another it manifests itself earliest in the lymphatic glands, or attacks the bones and joints from the very first. This irregularity in the succession of symptoms and in the selection of definite localities is much more marked in our disease than in hereditary syphilis, although this also presents not a few irregularities in this respect.

One must not believe, therefore, that in every case of scrofulosis of long duration the severer forms must follow the lighter ones ; in some cases of many years' standing, nothing but affections of the skin and mucous membrane are found frequently enough ; and equally erroneous would it be to infer from the presence of severer affections the previous existence of lighter ones.

It is certainly probable that hygienic conditions, as well as acquired or inherited power of the several kinds of tissue to resist morbific agents, exert a certain kind of influence on the respective course of the disease; but these are factors of which we cannot form an accurate estimate.

Although the course of the disease is not a typical one, it is, nevertheless, convenient to collect the morbid appearances in definite groups, according to their severity and localization. In those cases in which the severer forms arise out of the lighter ones, the different groups would at the same time correspond to certain stages of the disease.

Eruptions on the skin and catarrhal affections of the mucous membranes are most frequently the first sign of scrofulosis. The former have their seat principally on the hairy scalp and in the face, while the latter invade the mucous membranes of the organs of special sense, and less frequently those of the respiratory and alimentary tract.

The affections of the skin are frequently, throughout the whole duration of the disease, or at least in the beginning, only superficial, but at the same time very persistent, and especially inclined to relapse. The behavior of the affections of the mucous membranes is similar. Swelling of the corresponding lymphatic glands is early associated with these peripheral processes. These tumefactions show at first, and frequently for a long time, no difference from ordinary swellings of the glands, the result of simple irritative processes.

These tumefactions, generally of small volume, disappear not infrequently as soon as the peripheral inflammatory processes cease.

The above-mentioned phenomena, which occur in the lighter forms of scrofula or in the earlier stages of the disease, have been comprised by Bazin as the *primary period*, and designated by the name of *scrofulides*.

The more malignant and obstinate course is mainly characterized by the greater severity of the glandular affection, which here loses the character of sympathetic swelling, and continues to develop even after the disappearance of the peripheral processes. The tumor increases to a considerable volume, the gland becomes hard, the several glands coalesce into a knotty bunch;

inflammation and suppuration take place frequently, while in other cases the tumefaction remains stationary for a long time, until finally softening sets in, the skin breaks, and scrofulous ulcers or fistulæ form. It is evident that in these severer cases the general nutrition must suffer, and a cachectic condition result. To these severe affections of the lymphatic glands, especially when occurring on the neck, corresponds the characteristic physiognomy described as belonging to the torpid type of scrofulosis.

Simultaneously with these more persisting affections of the lymphatic glands, more deep-seated affections of the skin appear, while the affections of the mucous membrane also become more obstinate and spreading. (Bazin describes these phenomena as the *secondary period.*)

The character of this stage of scrofulosis is dangerous enough, and threatens the whole constitution in more than one respect, but the scrofulous affections attacking the osseous system are still more severe. Obstinate arthritis, periostitis, osteitis (caries necrotica), must be mentioned here (Bazin's *third period*).

Besides the already mentioned disorders, finally, severe affections of the internal organs (pulmonary consumption), disturbances of the general nutrition (amyloid degeneration, etc.) set in, and, as a rule, the fatal termination of scrofulosis is brought about by secondary processes (Bazin's *fourth period*).

We have already pointed out that the succession of symptoms in the course of scrofulosis is not to be represented by any systematic order. In any individual case the above described stages may be recognized to a certain degree, but the general course of the disease is not a continuous one; on the contrary, it is characterized by an irregular change of the symptoms, which abate from time to time, or sometimes even disappear so completely that the hope is entertained of an improvement in the patient's constitution amounting to an extinction of the disease. Suddenly, and often without any assignable cause, the severest symptoms reappear, destroying by their intractability all illusions as to the success attained by dietetic or medicinal treatment. Sometimes it is the same group of symptoms which, during the whole course of the disease, reappears with ever-changing exacerbations and remissions; sometimes a new group presents itself after the disappearance of the old one, and often the impression is created of a downright antagonism between the affections which succeed each other.

I have for the last three years under my treatment a scrofulous girl, twelve years old, who from time to time is troubled with ophthalmia, coryza, and eczema of the face of great severity. In this case I could repeatedly observe painful tumefaction to a considerable extent of the cervical lymphatic glands (especially near the angles of the jaw), whenever those phenomena receded. As soon as the first symptoms exacerbated, an evident remission of the glandular swelling, and especially of the pain in it, took place, and, strange to say, the general condition always improved with this remission. That this was not a mere coincidence is proved by the repeated occurrence of this alternation of symptoms, it being observed not less than five times in the course of a single year. Similar facts are reported by other observers.

The course of scrofulosis is generally a chronic one, the respective affections showing little tendency towards recovery, or a new group of symptoms taking the place of a disappearing one, but it cannot be denied after all that sometimes an *acute* course of it is observed. When a child, whose parents have previously suffered from scrofulosis, is suddenly attacked by conjunctivitis and external otitis, by coryza and eczema of the face, combined with conspicuous swelling of the cervical glands, we shall not doubt for a moment that this child is scrofulous, and not retract this opinion even if we find that all these symptoms disappear again after the lapse of a few weeks and the child remains for years afterwards free from all scrofulous affections. Such cases, which are not so very rarely observed in practice, would almost seem to justify the term "scrofula fugax," but we ought not to comprehend under this name, as was done by its originator, all transitory tumefactions of the lymphatic glands.

Pathological Anatomy.

In treating of the pathogenesis of scrofulosis we have already mentioned several of the anatomical changes accompanying it. The same has been done in other parts of this work.[1] We shall, therefore, enter into a more detailed discussion of only a few of those changes.

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[1] Vol. V.

The superficial affections of the skin and mucous membranes of scrofulous subjects do not present a peculiar anatomical character.

The abundance of cells in the secretions and the dense cellular infiltration of the parenchymatous connective tissue of the mucous membrane, which Rindfleisch[1] considers to be a characteristic feature of scrofulous catarrh, are also found in chronic inflammations of the mucous membrane arising on a non-scrofulous basis. Neither is the presence of tubercles in the more deep-seated inflammations, which lead to ulceration, peculiar to scrofulosis, although it cannot be denied that the formation of tubercles at the bottom and around the margin of these ulcers is almost never wanting in scrofulous patients. But we have already mentioned that tubercles appear also in chronic ulcers which owe their origin to very different causes (syphilitic ulcers, erosions on the os uteri, etc.), and local tuberculosis must therefore not be considered as identical with scrofulosis.

The deep lesion of the skin which we designate as *lupus*, and which occurs in the otherwise healthy as well as in the scrofulous, is equally devoid of a specific character when affecting the latter. It is well known that Friedlaender has demonstrated in all forms of lupus a proliferation of tissue which exactly corresponds to the nature of tubercle.

The question, whether tubercles occur in these cases primarily or develop secondarily, need not be discussed here, but it is clear from what has been said above that the presence of tubercles cannot be considered as the characteristic sign of the lupous skin affection of the *scrofulous.*

As these scrofulous affections are devoid of any specific anatomical changes, we need not here refer to them in detail.

The scrofulous *tumors of the lymphatic glands* present two stages even on ordinary inspection. In the first the glands are moderately swelled, rarely exceeding the size of a filbert, of an elastic, moderately firm consistence, rarely soft, and not coalescing with each other.

Opportunities to make a histological examination of the glands, in this stage, are on the whole very rare. The dead bodies of scrofulous patients show, it is true, newly affected glands by the side of those in a state of advanced change, but we cannot suppose without further evidence that the former represent a true picture of the condition in which the latter were during the previous stages of the disease. If, for example, tubercles are developed in the glands of more peripheral position, the more central ones may become infected by them, or in other words, the appearance of miliary tubercles may be the first change in the latter glands, and we are certainly not justified in concluding therefrom that, in the glands first attacked, tubercles also appeared from the very beginning of the morbid change.

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[1] L. c.

We may assume this first stage to consist in a hyperplasia of the gland constituents, set up by some conducted irritation, with all the greater certainty the more frequently the clinical history of such tumors can be interpreted in favor of such an opinion. On the other hand, opportunities are not altogether wanting to demonstrate, on the post-mortem table, the occurrence of simple hyperplastic glandular tumors in scrofulous subjects.

Schueppel, who is a strong advocate of the characteristic significance of tubercles for the scrofulous glandular affection, published a case in which he saw scrofulous tumefaction of the glands in the first stage; in this case he found only simple hyperplasia, no development of tubercles and no cheesy degeneration.[1] The author made a similar observation on the body of a child, five years of age, which had died of meningitis following otitis media. This child had suffered also from other scrofulous symptoms (eczema, conjunctivitis). The cervical lymphatic glands were increased in bulk to the size of a filbert, rather soft, succulent, and of a grayish-red color. Microscopical examination showed enormous cell proliferation in these and the mesenteric glands, the cells in the follicles forming globular clusters without any intercellular substance, and the lymph sinuses being visibly compressed.

Facts of this kind support the opinion that at least in many cases, especially when formation of tubercles has not yet taken place in the periphery, the first stages of scrofulous tumefaction of the glands are of a hyperplastic nature.

The second stage of the changes is characterized by the beginning of *cheesy degeneration.* The glands increase still more in size, become hard and less elastic, and present on section the cheesy material at first in discrete clusters imbedded in gray or grayish-red substance. Later on the enlarged gland becomes cheesy throughout its whole extent and is transformed into a homogeneous dry yellow mass, which has been compared already by de Haen to a bisected potato. On *microscopical* examination of the parts in a state of complete cheesy degeneration, we find irregular globular corpuscles, shrivelled nuclei and cells, and here and there larger flaky elements which may be claimed as giant-cells. In glands, however, which contain also gray portions besides the cheesy ones, we see, *almost without exception, well-characterized tubercles in the follicular substance* (giant-cells, and a network, the wide meshes of which are filled in with epithelioidal cells). In such portions the tubercles are often seen even with the unarmed eye, as fine yellowish-gray dots. The remaining tissue of these portions is distinctly hyperplastic; the sinuses are more or less compressed.

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[1] L. c., page 27.

The formation of the cheesy masses is, according to Virchow's opinion, owing to necrobiosis of the hyperplastic constituent elements of the lymphatic glands, while Schueppel thinks it can be brought about only by means of tubercular development.

It is conceded by Schueppel that the appearance of the cheesy substance does not of itself show us, as a rule, from what tissue it has arisen. The reasons on which he founds his view of the tuberculous origin of the cheesy material are essentially as follows:[1] In the cheesy substance giant-cells are frequently found which, according to his experience, occur, *without exception*, as integral parts of tubercle in the glands. To this reason we may oppose the fact that such cells are not found in all cases, and the consideration that, even admitting the positive proof of the existence of such elements in individual cases, part of the cheesy material might have been formed out of hyperplastic tissue. Finally, it may be doubted whether it be true that giant-cells occur in lymphatic glands only as a result of tuberculosis.

His second reason is founded on the occurrence of innumerable tubercles in glands which did not show any signs of cheesy degeneration. This fact, however, can only prove that extensive tuberculosis of the lymphatic glands may exist without cheesy degeneration, but by no means that every case of cheesy degeneration in the lymphatic glands is the result of tuberculosis; and it is still less capable of furnishing such proof, as already mentioned, if tubercles occur in glands secondarily affected.

Our experience with other diseases shows us, furthermore, beyond doubt, that simple hyperplastic lymphatic tumors may undergo cheesy degeneration; we have in this respect only to refer to typhoid swellings of the glands. A comparison of the different behavior of *secondarily tuberculous* and scrofulous glands also speaks in favor of the opinion that hyperplastic processes play a part in the cheesy degeneration of the latter aside from the development of tubercles.

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[1] L. c , page 113.

In secondary tuberculous glands (for example the mesenteric glands in tuberculosis of the intestine) the tumefaction is less considerable, and the cheesy substance mostly deposited only in the form of discrete foci. On microscopical examination we accordingly find the nodules, mostly occurring in the follicular substance and less frequently in the capsule, embedded in a relatively normal lymphatic gland tissue. The sinuses are compressed either not at all or inconsiderably. The contrary is seen in the general hyperplasia of scrofulous glands in which the sinuses are frequently found blocked up by necrotic masses, a circumstance which shows that the contents of the latter also are bound to undergo cheesy necrobiosis. In conformity with this condition we can easily inject by puncture the sinus-channels of secondarily tuberculous glands, while it is difficult or impossible to do so in scrofulous lymphoma.

The nodules appearing in the interior of the follicles of hyperplastic glands, and originating from the dense agglomeration of lymph-cells at the expense of the rarefied reticulum, have been mentioned before. These nodules, which may be discerned by the unarmed eye as fine dots of white or yellowish color, and are easily removed from the cut surface by a gentle stream of water, not infrequently present in their cellular elements evident signs of retrogressive metamorphosis and are liable, as it seems probable *a priori*, to cheesy degeneration.

This has been proved by the observations of Armauer-Hansen,[1] and the author had also occasion to find in the lymphatic glands of a scrofulous subject which presented no tubercles anywhere, such nodules with their elements in a state of metamorphosis by the side of others showing little alteration, and in other portions again minute cheesy foci whose mode of distribution exactly corresponded to these nodules.

In view of these facts we must believe it possible that cheesy degeneration of scrofulous lymphatic glands does not exclusively take place by mediation of tuberculosis, although we have to grant that it is an exception to find glands containing cheesy material for examination in which tubercles cannot be discovered.

Among ten cases of extirpation of lymphatic glands from the neck of scrofulous individuals, the author discovered tubercles in nine, but every one of them also showed hyperplastic processes.

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[1] Beiträge zur path. Anat. der Lymphdrüsen. S. 41.

The constant occurrence of this result shows clearly that at a certain stage of the disease local tuberculosis is regularly developed in the lymphatic glands of scrofulous persons. Among the further changes of the glands in the state of cheesy degeneration *softening* is one of the most important. The dead parts are liquefied, a purulent fluid mixed with cheesy débris results, and thus scrofulous caverns are formed, which, after discharging their contents outwards, become scrofulous ulcers. Not infrequently softening is accompanied by inflammatory processes in the neighborhood of the glands, several of which coalesce simultaneously into voluminous knotty bunches, and occasionally regular suppuration and formation of abscess occurs in the vicinity of the affected glands. Clinical observation furnishes not a few instances of the disappearance, without breaking, of scrofulous glandular tumors, the size and consistence of which make us suppose that cheesy degeneration has already taken place in them; it seems, therefore, probable that the cheesy substance, too, is capable of absorption, as Virchow thinks, by means of gradual softening proceeding from the periphery toward the centre.

At the bottom of the scrofulous ulcers arising from the breaking of the glands, and in the connective tissue of their vicinity, tubercles are also developed in all cases; on the formation of sound granulations they again disappear, and the ulcer heals, forming one of those well-known radiating, often depressed or not unfrequently hypertrophied cicatrices.

Less frequently the cheesy glands remain for a long time stationary or diminish but little in volume, undergo calcification and become dead parts of the body surrounded by capsules, the product of proliferating connective tissue around them.

Another form which the lymphatic glands may assume has already been mentioned.

On the neck and in the region of the parotis, but especially on the former, glandular tumors occur in young people which differ from indolent syphilitic buboes by their size, often attaining that of a goose's egg, and from the ordinary scrofulous tumors by showing little tendency to cheesy degeneration.

Price, who was the first to describe these tumors, regards them as hypertrophied glands.

Virchow[1] also classifies them with the simple hyperplastic lymphomas. They present partly a homogeneous fleshy structure, partly a granulated appearance. In the interspersed granular substance Virchow found flat nucleated cells of epithelium-like appearance and multinucleated giant-cells. According to our present more accurate knowledge of the structure of the tubercles of lymphatic glands, these granules must be classified with the tubercle, as is done by Schueppel, the distinguishing feature of these tubercle-bearing lymphomas being the want of cheesy degeneration.

As these glandular tumors are not rarely found in people who do not present any other symptoms of scrofulosis, it may appear doubtful whether they may justly be classified with the scrofulous affections of glands. That we are not justified in interpreting the occurrence of tubercles in this sense has already been pointed out. One is tempted to ask whether we have not to deal in this case with primary tuberculosis of the lymphatic glands developing itself independently of scrofulosis.

Beside the abscesses forming in the vicinity of scrofulous glands, which reach the surface by a direct or circuitous route, others are found not infrequently in scrofulous persons, especially in the subcutaneous connective tissue, in the vicinity of bones, etc. These accumulations of pus frequently appear in the shape of so-called *cold abscesses* (lymph abscesses). They contain a thin watery pus deficient in pus corpuscles and mixed with flaky coagula, are rather frequently surrounded by a capsule, and extend more or less into the connective tissue, according to the influence of gravity and the nature of the obstacles which they meet with on their progress. After breaking they give rise to the formation of scrofulous ulcers, which assume a considerable circumference, especially when the skin has been extensively undermined; frequently they are associated with affections of the bones.

Acute suppurations of ordinary character may, however, arise in scrofulous subjects at any time.

The scrofulous *affections of the joints* have no specific anatomical character, as little as other inflammations arising under the influence of scrofulosis; they may occur exactly in the same manner in non-scrofulous subjects.

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[1] Geschwülste, II., page 617.

In former times two forms of this affection were described, *Arthrocace* and *White Swelling;* for the latter term, which, by the by, was used for all swellings of the joints unaccompanied by redness of the skin, that of *Fungous Arthritis* has been substituted, and at present pretty generally accepted.

If it seems desirable to give a special meaning to the term *Arthrocace*, this name may best be given to those affections of joints in which the bones—that is to say, their articular extremities—are essentially involved. No fundamental difference is, however, established thereby, as one form of the disease may be evolved from the other.

The anatomical changes accompanying these inflammations are various according to the character of the latter, which may be a simple fungous inflammation, or one accompanied with suppuration and ulceration (caries). We may therefore distinguish a purulent ulcerating and a fungous inflammation in the stricter sense—a distinction, however, which will always be of a somewhat theoretical nature, considering that these processes are frequently combined. If the inflammation begins in the joint itself, the synovial membrane will at first become red and swollen, and then covered with spongy granulations which grow from the sides over the whole surface of the cartilage, insinuating themselves between the articular extremities (Synovitis granulosa). The capsule of the joint becomes thickened at the same time, and assumes a lardaceous appearance; the neighboring connective tissue (of the tendons, fasciæ, the periosteum and subcutaneous tissue) is similarly involved. Later on the granulations which cover the cartilage invade its substance and cause its absorption; finally caries of the articular extremities of the bones joins the fungous arthritis (Arthrocace). The order of these processes may, however, be reversed; ostitis of the articular processes may arise first, lead to ulceration in the next place, and then be followed by secondary arthritis. The suppuration is not an absolutely necessary element of fungous arthritis; frequently only small quantities of muco-pus are found with extensive development of the spongy granulation tissue.

In other cases suppuration takes place very early, while the granulations are but sparingly developed, in the joint and its vicinity (periarticular abscesses, which, however, occur in the scrofulous, not infrequently without inflammation of the joint itself).

The ulterior consequences which may follow the destruction of the capsule and the articular processes (perforation, formation of fistulæ, luxation, changes in the muscles, etc.) cannot be described here in detail; in this respect, and regarding the special description of the diseases of the bones occurring in these affections, the reader is referred to the respective chapters in text-books on pathological anatomy and surgery.

One of the minute anatomical features of fungous arthritis, however, deserves special notice: the occurrence of tubercles in the spongy granulations, discovered by Koester.[1] These tubercles have their seat almost exclusively in the newly-formed granulations—a fact which furnishes additional proof that tuberculosis is a secondary process associated with inflammation. The tubercles are not only found in the joint, but also in the granulation-tissue of the surrounding parts, in the fistulous tracts, etc., and show greater tendency to fatty metamorphosis than to cheesy degeneration. Regarding the character of the inflammation, certain differences are presented by the several joints: in the hip-joint caries and suppuration are most frequent (Coxarthrocace); in the knee-joint simple fungous inflammation (tumor albus genu) predominates, etc.

The *affections of the bones* in the scrofulous show the same character as those of the joints. Inflammations of the *periosteum* occur in the scrofulous independently of, or associated with, affections of the bones and joints.

Acute periostitis does not present any peculiar features, attacks pre-eminently the long bones, especially those of the lower extremity, runs its course with or without suppuration, and leads, in the former case, frequently to necrosis. *Chronic* periostitis may occur as ossifying, fungous, or suppurative inflammation; most frequently there is a combination of all these processes. Tubercles may be demonstrated also in the spongy granulations of the periosteum.

The fungous or fungo-purulent periostitis is almost without exception joined by ostitis (caries). Here, too, we have to deal with forms which are equivalent to the above-described varieties of arthritis. Fungous caries, in which the bone is worn off by the interstitial development of spongy granulations, is frequently observed in scrofulous subjects. In broken-down individuals —that is to say, in the later stages of the disease—atonic caries appears, characterized by a deficient development of granulations. This shows greater tendency to necrosis and cheesy degeneration of the products of inflammation. In these cases, also, tubercles are almost always found among the granulations.

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[1] Virch. Archiv. XLVIII. p. 95.

Primary chronic ostitis (resp. osteo-myelitis) affects especially the spongy substance of the bones, principally of the vertebræ, the short bones of the extremities, and the epiphyses of the long bones The most frequent form of this affection also begins with the development of spongy granulations from the vessels which cause enlargement of the medullary spaces and absorption of the osseous trabeculæ. Sometimes suppuration (abscess of bone), formation of fistulæ, and necrosis of extensive portions of bone take place at an early period. In other cases suppuration is wanting; the bone is, so to speak, substituted by the luxuriating mass of granulations (caries carnosa), and finally retrogressive metamorphosis occurs in not a few instances. Then cheesy masses are found deposited in the bone, which also may undergo softening, and thereby lead to extensive destruction. These cases which end in cheesy degeneration (ostitis interna caseosa) have principally furnished the material for Nélaton's description of *osseous tubercles*. Although we look upon these cheesy foci as mainly arising from necrosed granulation-tissue, we must, nevertheless, concede that real tubercle nodules are frequently met with in the vicinity of them. In the most severe cases all the described forms of diseases of joints, periosteum, and bones are found combined.

Of scrofulous affections of other organs we have yet to mention the cheesy inflammations of the lungs, brain, testicle, etc. We have already said that not every pulmonary disease ending in cheesy degeneration is to be recognized as scrofulous, but we cannot deny on the other hand that inflammations of the lungs ending with a cheesy deposit and leading to phthisis are frequent among scrofulous children, and must also admit that such cases owe their origin to a scrofulous constitution. This cheesy pneumonia of scrofulous subjects, however, does not present any anatomical differences from analogous local processes developed on a different basis. The existence of tubercles has of late been demonstrated also in nearly all these cases, and the discussion does no more refer to this fact, but to the question whether the tubercles found be of primary or secondary origin. As to the details of this subject we refer to the respective chapters of this work.

The cheesy encephalitis which takes its origin principally in the cerebellum of scrofulous children has a still closer relation to scrofulosis than cheesy pneumonia has. It is still undecided whether this affection, which appears in the form of cheesy nodes, attaining and even exceeding the size of a large walnut, is to be considered as a conglomeration of tubercles or as an inflammation leading to cheesy deposit with peripheral tubercular eruption.

The same may be said of similar processes taking place in other organs; they are found on the basis of a scrofulous constitution and combined with other homologous affections, or they are developed singly under local circumstances or as effects of general causes of a different nature.

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Symptomatology.

If we intended to describe all the phenomena arising under the influence of scrofulosis we would have to go over a very extensive portion of pathology, for the number and variety of these phenomena is very great; and such an attempt would lead us to fields which belong partly to the domain of surgery and partly to that of special departments (ophthalmology and otiatrics). Such detailed treatment would transgress the scope and limits of this treatise too far, and we must therefore content ourselves with a general outline of the forms of symptomatic phenomena appearing in the several organs of those afflicted with scrofulosis.

The *scrofulous skin diseases* do not essentially differ in their forms from the cutaneous affections developing themselves independently of scrofulosis. A certain peculiarity as to the frequency with which their several forms occur in the scrofulous must, however, be conceded, inasmuch as certain skin diseases do not show themselves more frequently on such persons than on the non-scrofulous, while others, again, exhibit a decided predilection for the scrofulous constitution. Regarding their seat, it is to be remarked that the scrofulous exanthemata most frequently occur on the hairy scalp and face. The peculiarly obstinate character of these cutaneous affections and their tendency to a chronic course and frequent relapses has already been adverted to above. These peculiarities, however, cannot sufficiently warrant a separate classification of scrofulous skin diseases as affections of a distinct kind, as attempted by Hardy,[1] and especially by Bazin; it is not expedient to speak of pustulous, squamous, tuberculous, or horny scrofulides, etc.[2]

In reference to the group of exudative cutaneous affections (Hebra's classification) running an acute course, we may perhaps remark that scrofulous subjects show a special liability to the formation of so-called *perniones* or chilblains—a form of dermatitis which in them is caused by relatively mild degrees of cold. Of the squamous group with a chronic course *psoriasis* is not more frequent in scrofulous than in non-scrofulous individuals, while another member of it, the *lichen scrofulosorum*, has, according to Hebra, a special relation to scrofulosis.

This skin-disease appears in the form of papules of the size of a millet seed, of a bright red or brownish-red color, or not differing in color from the surrounding epidermis, always standing out in groups (sometimes of a circular shape); they persist for a long time and do not undergo any change, except that of gradual exfoliation and involution. They are seated mostly on the trunk, very seldom on the extremities. The papules itch very little. As a rule, they break out in many groups or all together at the same time, soon reach their greatest development, and remain unchanged for a long time. Their first appearance is generally overlooked, being unaccompanied with pain. Between the groups of papules, but also in other places (on the extremities and face) discrete red buttons frequently appear, of the size of a lentil, which resemble common acne, and some of which contain pus. Over the several efflorescences desquamation takes place in the form of branlike scales of dull lustre. Repeated eruptions of papules may succeed each other for a long time, and thus the disease lasts for years without interruption. The relation of this cutaneous affection to our disease is best shown by the fact that Hebra observed ninety per cent. of the cases in young individuals who presented at the same time considerable swelling of the lymphatic glands or suffered from periostitis, caries, and necrosis, with or without scrofulous ulcers of the skin, or finally in patients whose tumid abdomen, bad nutrition, and cachectic appearance pointed to the existence of disease of the mesenteric glands. In no case, however, could symptoms be found indicating pulmonary tuberculosis.

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[1] Des différentes formes des scrofules cutanées ou scrofulides. Gaz. des Hôp. 1854. No. 115.

[2] *Fuchs* ascribes to scrofulous affections of the skin a peculiar bluish-rosy color, a specific odor resembling that of cat's urine, and a special tendency to the formation of œdematous swellings in the affected portions of the skin.

From *lichen ruber* the lichen scrofulosorum is distinguished by the position and color of the papules, and by the duration of the disease; from *papulous eczemas*, especially by the absence of itching.

According to Kaposi's investigations the lichen scrofulosorum consists anatomically in a cell-infiltration around and within the hair-follicles, their sebaceous glands, and the papillæ surrounding the mouths of the follicles.

It is a striking fact that this cutaneous affection has so far been observed exclusively in male individuals at the age of from ten to twenty-five years. Lichen scrofulosorum must not be confounded with the eruption known as pityriasis tabescentium, scrofulosorum, or tuberculosorum which generally occurs in emaciated individuals broken down by any chronic disease; this consists in a general seborrhœa, and appears in the shape of fine branlike scales, especially on the skin of the trunk. In patients afflicted with severe forms of scrofulosis, especially diseases of the bones, this pityriasis tabescentium is frequently developed.

Eczema is the most frequent form of cutaneous diseases occurring in the scrofulous. As defined by Hebra, this disease, most frequently running a chronic course, is characterized by the formation of papules and vesicles in clusters, or by more or less reddened patches covered with thin scales or serous exudation, or in other cases, which formerly were designated as crusta lactea or by some other name, by yellow gum-like or green and brown scabs. These latter cases are of most frequent occurrence in scrofulous subjects. Another characteristic symptom of eczema is intense itching.

The favorite seat of the impetiginous form of eczema, the most frequent in scrofulosis, is the hairy scalp, but it may also occur on the ears and their vicinity (associated with otorrhœa), on the eyelids (sometimes invading the hair-follicles, eczematous blepharitis) or in the neighborhood of the nose.[1]

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[1] Of *Lebert's* 116 cases of scrofulous skin diseases 91 were found on the head and face.

On the cheeks of scrofulous individuals are often found those beautifully yellow scabs resembling dried honey, which Alibert described under the special name of melitagra flavescens. Of the other cutaneous diseases we mention *prurigo*, which not infrequently appears in children, particularly of the poorer classes, although it may be seen also in children presenting no signs of scrofulosis. The circumstance that the mothers of children afflicted with prurigo are generally tuberculous, would seem to indicate, however, a certain internal connection between this skin-disease and scrofulosis.

Those cutaneous affections which were formerly called *impetigo*, are at present classified as eczema impetiginosum. The distinct character of the pustulous eruptions known as *ecthyma* is equally doubtful, while *rupia*, although occurring associated with scrofulous symptoms, is only found in cases in which the existence of constitutional syphilis may be suspected.

It has already been mentioned above that no definite relation to scrofulosis can be claimed for *lupus* in general or any of its several forms, although it is not denied that lupous affections of the skin are not rarely found in scrofulous individuals. It is a remarkable fact that lupus, when occurring without any such complication, runs its course unaccompanied by swelling of the neighboring lymphatic glands; and not less striking is the very rare occurrence of tubercular disease of the lungs among patients suffering from lupus.

Of the scrofulous ulcer we shall speak more fully hereafter.

The *scrofulous affections of the mucous membranes and the organs of special sense.*—As a general rule, the scrofulous disorders of the mucous membranes are of a catarrhal nature, furnishing mostly a profuse, comparatively thick secretion, which readily dries and shows great capacity for irritating the skin at all points of contact (at the entrance to the organs of special sense), easily causing erythema and eczema. This quality of the secretion furnished to the ancient authors the reason for assuming a specific scrofulous, acrimonious humor. The *mucous membrane of the nose* is the most frequent seat of the disease which here assumes the character of a regular eczema; the nares are filled up by thick yellow crusts, beneath which the membrane is superficially eroded, the nose becomes swollen, and thickening of the upper lip is produced by the irritation of the secretion flowing from the nose (scrofulous physiognomy). The scrofulous coryza persists for a long time, presents various changes of intensity and frequent relapses after apparent recovery. Deeper lesions, leading to periostitis and caries (ozæna scrofulosa) are, however, rare. The external meatus of the ear is similarly affected; *otorrhœa* is one of the first symptoms of scrofulosis, it may be of either mucous or purulent character, and is apt to be associated with eczema of the auricle; cases in which this external otitis extends directly to the deeper parts, causes abscesses, destroys the membrana tympani, and attacks the middle ear, are, however, relatively rare. *Otitis media* occurs, as a rule, independently of inflammation of the external meatus, and by extension of the catarrhal affection of the nose and mouth through the mediation of the tubes. An insignificant complaint in its milder degrees, catarrhal otitis media must, nevertheless, always be regarded with distrust, as it may suddenly, and in many cases after an existence of several years, assume a purulent character, and then be followed by the grave consequences of purulent otitis media which, in the most favorable case (bursting of the abscess on the surface, especially after perforation of the membrana tympani), leaves behind a considerable disturbance of the function of hearing, while in less favorable cases it may lead to necrosis of the petrous portion of the temporal bone, to meningitis, cerebral abscess, or even to the development of fulminating pyæmia (by means of thrombosis of the sinuses). However rarely these grave consequences may occur, the importance of the scrofulous affections of the ear is sufficiently demonstrated by the observation that scrofulosis is at the bottom of the largest number of cases in which weakening or destruction of the function of hearing has taken place during the age of childhood. The large number of scrofulous individuals found in deaf and dumb asylums is to be explained by these facts.

Another affection frequently occurring in the scrofulous is *ophthalmia.* The hypothesis of a specific scrofulous inflammation has been first discarded in reference to this very disease, the specific character of which was asserted by the older authors on the ground of its tendency to matutinal exacerbations, of the excessive photophobia, and certain anatomical characters presented by it. Referring the reader to the text-books on diseases of the eye for a detailed description of it, we shall only point out its essential characteristics.

The *eyelids* are pretty frequently the seat of inflammation in scrofulous subjects. Eczema of the face is especially apt to extend to them, and cicatricial contractions, entropion, ectropion, abnormal position of the eyelashes, etc., may result from the spread of the inflammation to the ciliary follicles and glands and their destruction by suppuration.

Most of the characteristics which formerly were regarded as specific symptoms of scrofulous ophthalmia, are derived from the *herpes conjunctivæ et corneæ;* at least it cannot be denied that these forms of disease are quite frequent among the scrofulous. It is in these affections especially that we find photophobia of a high intensity, frequently out of all proportion to the slight extent of the conjunctival or corneal disorder, spasm of the lids and profuse lachrymation; the development of that circumscribed keratitis vasculosa, which extends to the seat of the eruption and corresponds to "the scrofulous vascular frenum" of the older authors, is also favored by this condition.

Although we sometimes observe herpetic inflammation of the conjunctiva and cornea originated by traumatic causes, we have nevertheless to acknowledge that these cases mostly run a mild and short course in non-scrofulous subjects, while those coupled with a scrofulous disposition are prolonged for weeks and months by the occurrence of fresh eruptions.

Stellwag von Carion[1] is of the opinion that herpes corneæ becomes a frequent cause of scrofulosis by the disturbances which it causes in the general condition of the body; whenever the signs of scrofulosis precede the herpetic affection, this is, according to his view, not to be regarded as a localization of the special blood-disease (?) but only as an effect of the erethism of the nervous system. The same author, moreover, points out the excessive intolerance of light with violent spasm of the eyelids from the very beginning of the disease as a characteristic symptom of herpes corneæ in children of the so-called erethic scrofulous habit, and adds that the suffusion may be very moderate (rosy border in the episclerotic space) and the efflorescence so insignificant that it is easily overlooked (scrofulous photophobia).

The possible termination of herpes in keratitis vasculosa and pannus or its transition into purulent keratitis, iritis, trachoma, etc., may be passed by without notice; we will only remark that in the majority of cases scrofulous ophthalmia ends favorably, in spite of its long duration and frequent relapses, the only remains of it found later in life being mostly slight opacities of the cornea, of small extent. If the cases with a favorable termination form the rule we may conclude the great frequency of scrofulous ophthalmia from the fact that scrofulosis takes a leading position among the causes of blindness.

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[1] Lehrb. der prakt. Augenheilk. 1867. p. 59.

In the institution for the blind of Saxony, the cases of blindness from scrofulous ophthalmia amount to six per cent. of the total number below twenty years of age; to ophthalmia neonatorum eighteen per cent. are ascribed.

The internal membranes of the eye are but rarely involved even in the gravest forms of scrofulous ophthalmia, and consequently the retina retains its sensibility to luminous impressions even in cases of extensive opacities of the cornea, staphyloma, etc.

This is said, of course, without reference to the secondary development of choroidal tubercles in cases of general miliary tuberculosis. We may here mention that the existence of these tubercles has been known much longer than is generally believed; Rudolphi[1] has already stated that he observed a large number of small, white, round swellings in the retina and chorioidea of a "scrofulous monkey."

The *mucous membrane of the mouth and pharynx* also participates in this general irritability of the mucous membranes in scrofulous individuals. Here are to be mentioned chronic catarrhal affections accompanied with increased salivation, frequently exacerbating cases of quinsy and hypertrophy of the tonsils so uncommonly frequent among scrofulous children.

We would not count among these the *angina scrofulosa*,[2] more recently so much discussed, especially by French authors. As has been pointed out by these authors themselves, this disease is often found in people who do not exhibit any symptoms of scrofulosis, and often under circumstances indicating syphilitic causes; it is unaccompanied by swelling of the lymphatic glands; its clinical and anatomical characters correspond in nearly all the described cases to lupus of the skin, with which it generally goes together, and in other cases the symptoms point to severe forms of syphilitic ulceration.[1] All these facts speak against attributing to this disease any relation to scrofulosis.

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[1] Handb. der Physiol. Vol. II. p. 76.

[2] *Hamilton* (Dublin Jour. of med. 1845); *Bazin*, *Desnos* (Diction. de med. 1866); *Isambert* (Soc. méd. des hopitaux. 1871); *Constantin Paul* (Gaz. hébdom. 1871. No. 47); *Landrieux* (Arch. gén. de méd. Dec. 1874. p. 660). Compare also Volume VII. of this Cyclopædia.

The *mucous membrane* of the *alimentary canal* is withdrawn from our immediate observation, yet it is possible to conclude, from the symptoms appearing in scrofulous subjects (dyspepsia, tumidity of the abdomen, constipation alternating with diarrhœa, mostly of a mucous character, loss of appetite alternating with voracious appetite), that the organs of digestion participate in the disease, and the tumefaction of the mesenteric glands often found in scrofulous subjects after death would also justify us in the supposition of an irritative process in the intestinal mucous membrane.

The *mucous membrane of the air-passages* is also exposed to frequent catarrhal affections in the scrofulous (bronchitis scrofulosa); this is especially the case with children of the so-called erethical habit. This circumstance deserves all the more attention because it leaves the impression that children of phthisical parents are principally affected in this way; hence, we may suppose in these cases, with some probability, the existence of a hereditary weakness, especially of the organs of respiration, which, however, may be found also independently of scrofulosis.

Of other affections of the mucous membranes, *blennorrhœa of the vagina* deserves to be mentioned, which occurs somewhat frequently in scrofulous girls; it is observed sometimes at a very early age—mostly, however, towards the age of puberty.

The character of the *scrofulous affections of lymphatic glands* may be inferred to a great extent from the anatomical descriptions already given above. The painless, moderate swelling, which is capable of simple resolution, is probably owing to a simple hyperplastic process. The more voluminous, harder tumefaction, in which the glands coalesce into larger bunches, corresponds to cheesy degeneration, which, as above described, is almost without exception associated with local tuberculosis. In this stage inflammation of the parts surrounding the gland is apt to supervene; the gland becomes painful, the skin over it loses its mobility to a great extent and gets reddened; sometimes at an early period peri-glandular abscesses form, which break on the surface. If, on the contrary, the breaking results from softening of the cheesy material of the gland, the skin over the corresponding region becomes thinned, assumes a bluish red tint, and finally breaks spontaneously. The skin surrounding the opening dies to a greater or lesser extent, the remains of the gland are exposed to view; in short, a scrofulous ulcer is formed, which is characterized by a foul, lardaceous bottom, and livid, mostly flaccid, more rarely infiltrated margins. As long as a portion of the degenerated gland remains, there is continual secretion of pus mixed with necrosed débris of the tissue, and at the bottom of the ulcer tubercles develop frequently which may cause further disintegration. In the majority of cases, however, and after separation of the cheesy mass, healthy granulations spring up, by means of which restoration of the lost substance takes place with formation of an irregular, generally somewhat depressed, not infrequently hypertrophied cicatrix. It is a striking fact that the general health may be very good even when these multiple glandular tumors exist for a long time.

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[1] Compare especially the case observed by *G. Homolle*, Des scrofulides graves de la muqueuse bucco-pharyng. Paris, 1875.

In other cases no ulcer forms; the glands diminish somewhat in size, yet remain for a long time stationary in the form of bulbous tumors of still considerable volume. In such cases we may often see a gradual extension of the disease to other glands, until finally a whole chain of such tumors exists (for example, from the angles of the jaw downward to the mediastinal glands); the invasion of a new cluster is, however, as a rule, accompanied by pain, reddening of the skin, and general febrile reaction.

In such instances nutrition generally begins to suffer early, and later on tuberculosis of the lungs ensues very often.

We have already mentioned that sometimes absorption of the lymphatic glands may take place when so degenerated, while in other cases incapsulation and calcification ensue (especially in the glands of the mesentery, more rarely in those of the neck).

The behavior of the external glandular tumors may, of course, be observed more directly; it has been mentioned already that the glands of the neck are much more frequently involved than those of the axillary, cubital, or inguinal region.

According to Balman's statistics the anterior and posterior cervical glands are diseased in 81, the axillary in 6, the inguinal in 7, the cubital in 5, and those at the knee-joint in 0.7 per cent. of all cases.

We have already stated it as our opinion that, in the majority of cases, the affection of the lymphatic glands must be ascribed to an irritation conveyed by the lymph from distal parts; regarding the cervical glands, such an irritation cannot be excluded with certainty in any case, as irritations of the corresponding peripheral parts are of only too great frequency.

The author observed in a boy four years old, whose father had been scrofulous during his childhood, tumefaction of the axillary glands of the right side as the first symptom of scrofulosis, without being able to discover the least peripheral affection of the corresponding extremity. The tumor broke after attaining the size of a goose's egg, the resulting scrofulous ulcer healed some weeks later, and, only after this had closed, other symptoms of scrofulosis (conjunctivitis, eczema of the face, and tumefaction of the cervical glands) showed themselves.

Of the diseases of internal lymphatic glands, those of the bronchial and mesenteric glands (so-called pectoral and abdominal scrofulæ) deserve special notice.

The former develop most frequently as an effect of chronic bronchitis, especially after an attack of measles or whooping-cough; tumors of the bronchial glands (although containing tubercles almost always after cheesy degeneration has taken place) may exist without tuberculosis of the lungs, while in other cases tuberculosis of the bronchial glands probably precedes that of the lungs. Tuberculosis of the bronchial glands does not produce distinct symptoms in minor degrees of glandular swelling; if the tumors attain a more considerable size, the consequent pressure on the bronchi and trachea may cause dyspnœa and tracheal râles. Barthez and Rilliet observed some cases in which considerably enlarged bronchial glands exerted pressure on the vena cava descendens, and thereby produced dilatation of the veins of the neck, cyanosis, and œdema of the face.

According to Guéneau de Mussy,[1] patients in the first stage of bronchial glandular swelling suffer from dry spasmodic cough, dyspnœa, and abnormal tenderness of the thorax in the region where the glands are situated (spontaneous pain along the intercostal nerves). When the glands have attained greater size, depression in the vicinity of the jugular fossa becomes apparent on inspiration. Percussion (behind, near the spinous processes) gives an abnormally dull sound from the fourth dorsal vertebra downward; on auscultation, loud bronchial breathing is said to be heard in circumscribed spaces corresponding to the clusters of glands, as these conduct the respiratory sound from the trachea or bronchi with great intensity, while again the breathing is heard abnormally weak over those portions of the lung which communicate with compressed bronchi. Softening of the cheesy material, and consequent emptying of the gland-caverns into the trachea or main bronchi, occur but rarely in these glands.

The author saw lately, in the dead body of a girl aged sixteen, whose neck showed scrofulous cicatrices, two perforations of this kind through which softened bronchial glands had discharged their contents into the bronchi; one of them had taken place in the right bronchus and caused fatal hemoptysis by erosion of a branch of the bronchial artery. In addition, tubercular infiltration of the lung in the state of cavernous disintegration was present in this case.

The cheesy degeneration of scrofulous *mesenteric glands* (which is also always accompanied with formation of tubercles) cannot be found out by palpation; it is merely inferred from the presence of dyspepsia, diarrhœa, tumidity of the abdomen, and emaciation, especially when scrofulous affections manifest themselves also in other organs. Here, too, softening of the tumors, with breaking into the peritoneal cavity (peritonitis) or into the intestinal canal, adhesion having taken place previously, is quite rare. In some cases in which the latter occurred, the softened cheesy material has been discovered in the stools.

Scrofulous abscesses partly proceed from the diseased glands, partly they develop from inflammation of the periosteum or bone, or they originate directly in the subcutaneous and intermuscular connective tissue. Their symptoms vary of course according to their causes and seat. In general they are apt to extend through wide regions of loose connective tissue, while they are not able to penetrate more solid organs. Consequently they often undermine extensive portions of skin, which itself shows very little tendency to inflammation and becomes thinner by slow degrees, until finally it breaks; but then, after discharge of the thin watery pus, sloughing of the undermined portions of skin occurs and extensive scrofulous ulcers result therefrom. When communication has been established between the cavity of the abscess and the external air, the pus gets sanious in many cases, fever sets in, which, while the abscess is still closed, is usually present only in a moderate degree, and not infrequently septicæmia is developed.

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[1] Gaz. hebdom. 1871. Nos. 29 and 30.

The consequences of scrofulosis show themselves in the severest form, however, as affections of the *osseous system;* and among these again the most important are the diseases of the joints, especially those forms which, following Billroth, we have designated as *fungous arthritis* and already described under the head of Pathological Anatomy.

We must content ourselves with making here only a few remarks on the symptomatology of these affections, those of the joints as well as those of the bones, and refer to the text-books on surgery[1] for further details.

The course of fungous arthritis is a chronic one often drawn out through many years, sometimes starting with an acute beginning characterized by a chill, high fever, and great restlessness, which symptoms not infrequently precede the rapidly developing swelling of the joint. In the majority of cases, however, the disease gradually develops from an insignificant beginning; only slight pain is felt in the joint, accompanied by some functional disturbances, which appear especially after rising from bed in the morning. During the first stage the disturbances are indeed so slight that the early development of the disease may be easily overlooked, and considerable changes already exist in the joint when it is recognized. This trifling importance of the symptoms belongs especially to that form of arthritis which takes its origin in the bone. In a more advanced stage of the disease, relapses or exacerbations are frequently observed, which are accompanied with general febrile reaction, and often may be referred to external causes (mechanical injuries).

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[1] Compare especially *Volkmann* (Handbuch der allg. und spec. Chirurgie von *Billroth-Pitha.* II. f. 1 Abth. Krankheiten der Bewegungsorgane).

According to its course different stages of fungous arthritis have been distinguished.

The first stage is characterized by the development of the tumor, the abnormal position of the bones composing the joint, the beginning of the shrinking of the limb, especially of the muscles. In the second stage these symptoms increase, suppuration and ulceration are added (articular and periarticular abscesses), with perforation of the capsule and its ulterior consequences. As suppuration or ulceration may predominate, the course is modified accordingly. From what has been said above, it may be inferred that these stages do not occur in every case of the inflammation; already during the first stage recovery may take place, and then only slight or no impairments of function are left behind—unfortunately, a very rare occurrence.

Even from the second stage a patient may recover; but anchylosis remains even in the most favorable case, and not rarely perforation of the capsule causes considerable dislocation (luxatio spontanea), which admits of no cure. Frequently enough, however, remission of the arthritic symptoms is followed by fresh exacerbation, and not rarely the inflammation of the joint is instrumental in bringing about a fatal termination.

It has been stated already that scrofulous arthritis affects boys more frequently than girls. Lebert found, among 119 cases of scrofulous joint-affections, 71 males and 48 female patients. The predominance of the male sex is undoubtedly owing to the greater frequency of mechanical injuries of the joints in boys.

Arthritis appears most frequently in the hip-joint (coxitis scrofulosa), in the knee (gonarthrocace, white swelling), in the ankle-joint (podarthrocace), and at the elbow (olecranarthrocace); the wrist- and shoulder-joint are rarely affected. The peculiar symptoms which belong to the individual inflammations according to their seat cannot be described here in detail.

Nor is it necessary to give a special description of the symptoms of scrofulous periostitis; they are partly the same as those of an ordinary acute or chronic periostitis, and partly they disappear completely among the more important ones of the disease in the bone with which chronic periostitis is almost without exception associated, whether it precedes that disease or follows it as a secondary consequence.

The *scrofulous inflammations of the bone* are, like the affections of joints, distinguished by tendency to a chronic course. The first symptom of superficial ostitis is a swelling on the diseased bone attended with little pain; the skin over it, being at first unchanged in appearance, looks bluish and attenuated; perforation takes place very gradually, and then frequently an ulcer forms on the site. The further consequences depend on the existence of only a superficial affection of the bone, or of extensive ulceration (caries).

When the seat of scrofulous ostitis is more central, the first symptoms of the disease are of a very vague character; the most frequent is pain, not of a severe degree, however, which sometimes completely disappears, but soon returns again. The disease manifests itself distinctly only through its later consequences.

In parts which have to support considerable weight, the bones infiltrated with cheesy substance or the products of softening may be, so to speak, crushed under the influence of gravitation; the consequent destruction of normal form and injury to neighboring organs under such circumstances form the most important feature of the disease in certain regions, especially in the vertebral column. In other parts (bones of the extremities) the disease invades the joints and starts inflammation in them, or it reaches the periosteum, causes periostitis and inflammation of the superincumbent soft parts, and the final result is here also the formation of fistulæ and ulcers, at the bottom of which the carious bone is exposed. In this manner regular panostitis may arise, and necrosis of extensive portions of bone ensue, while all imaginable forms of inflammation coexist in the remaining tissues.

Although recognizing scrofulous ostitis as one of the gravest forms in which scrofulosis appears, we must not think a favorable termination impossible even when it is developed to the worst degree. This is especially to be hoped for in the case of younger children. Healthy granulations form gradually which cover the bone, suppuration diminishes, the ulcer closes, and even the bone, gravely affected as it was, reassumes its natural condition, and the loss of substance it has sustained is replaced by new osseous tissue.

Without going into details as to the several localizations, we will only point out the importance of the *destructive spondylitis* (spondylarthrocace). The disease is ushered in by pain increased by motion, but generally not by pressure on the spinous processes; later on febrile symptoms appear as a rule; sleep becomes disturbed; and not rarely, it is asserted, an impairment of the intellectual faculties is observed in such children. Later still the spinous processes become more prominent at the seat of the disease, the deformity gradually develops more and more, and the hump is formed (*Malum Pottii*). More rarely it happens that the diseased vertebra breaks down suddenly in consequence of some injury, and an angular bend is formed.

Whether kyphosis develop gradually or arise suddenly, symptoms of disturbed function of the spinal marrow manifest themselves immediately (more pronounced in the latter case, of course); they are, as may be imagined, different according to the seat of the trouble. In *spondylitis lumbalis*, which occurs more rarely, sciatica is present from the very beginning; the patient rises only with difficulty and supports the nates with the hands in doing so. If the disease is located higher up (*spondylitis thoracica*), pain, numbness, and formication are felt in the legs, sometimes associated with spasms, and later on paralysis of the lower extremities, the bladder, and rectum appears in severe cases. In *spondylitis cervicalis*, finally, disorders of the upper extremities (spasmodic and paralytic symptoms and difficulty of deglutition, vocalization, and respiration) are added when the disease is located in the occiput. In these cases considerable swelling of the posterior cervical region (tumor albus nuchæ) exists. If seated at the first or second cervical vertebra, the disease is, of course, most dangerous; in these cases violent headache is felt, fatal compression of the medulla oblongata may result from luxation of the first cervical vertebra, and another danger arises from extension of the inflammatory process to the meninges and the brain.

One of the most important accompaniments of spondylitis are the *burrowing abscesses* arising from suppuration in the vicinity of the diseased vertebræ; the presence of these does not, however, warrant in every case the diagnosis of an already existing spondylitis, because ante- or sub-periosteal suppurations, which may cause the formation of cold abscesses, do occur in this region without this complication. The direction in which these abscesses burrow differs according to the place of origin. Spondylitis lumbalis leads principally to abscesses which burrow along the pelvic organs, and reach the external surface through the sciatic notches; very seldom they break into the rectum or keep moving through the connective tissue in its vicinity. Thoracic spondylitis (especially of the lower thoracic and upper lumbar vertebræ) gives rise to abscesses, which follow the course of the psoas muscle, and make their appearance on the surface below Poupart's ligament. Finally, spondylitis cervicalis leads to the formation of retro-pharyngeal abscesses; more rarely the pus descends from that locality into the cavity of the thorax, etc.

The dangers of spondylitis may be concluded from the above description; functional disturbance of the spinal marrow, consumption of the body by the long-continued suppuration, putrid decomposition, which not unfrequently takes place in the abscesses after breaking—all these may severally cause a fatal termination. On the other hand, it is well known that even far advanced cases of spondylitis may be arrested in their progress; the deformity of the vertebral column remains, of course, but, through the mediation of ossifying periostitis, osseous trabeculæ are formed, which give a firm support to the dislocated vertebræ, capsules form around the cheesy masses in the bodies of the vertebræ, and part of the destroyed bone is restored. The abscesses, too, may be absorbed, or at least a capsule may form around the inspissated pus. The patients may enjoy good health, setting aside the usually existing diminution of motive power in those parts, the nerves of which arise from below the seat of the disease, and also the other disorders connected with kyphosis (deformed thorax, impaired circulation and respiration); it is, however, sufficiently explained by the circumstances alluded to that such individuals remain feeble, and rarely attain an advanced age.

Acute *osteomyelitis* does not occur more frequently in scrofulous than in healthy young individuals. We have, however, to mention another affection of the osseous system which almost exclusively occurs in scrofulous children mostly under five years of age. This is the peculiar disease which is now designated by the name of *spina ventosa*, while formerly this was applied to every possible morbid process in bone accompanied with swelling.[1]

The phalanges of the fingers and toes are the principal seats of this disease; more rarely the bones of the carpus and tarsus are affected. The characteristic sign of the process is a gradual, painless swelling of the affected bone—the phalanges of the fingers, for example, assume the shape of a bottle, and the skin over the swelling is frequently not reddened at all, but pale and tense. In some cases the swelling simply recedes; in others, abscess forms in the surrounding parts, the skin becomes red, and the abscess breaks. In some cases the probe, introduced through the spontaneous opening in skin and bone, reaches the medullary cavity; rarely, formation of an extensive sequestrum takes place. Accurate anatomical investigations of this process are still wanting, but it seems probable that spina ventosa is caused by a rarefying ostitis, with which ossifying periostitis is associated, and the bony substance absorbed through the pressure of proliferating marrow-cells is substituted by a new formation of successive involucra.

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[1] Comp. *Virchow* (Virch. Arch. XV. p. 210).

The clinical symptoms of the *cheesy and tuberculous inflammations* developing in the *internal organs* of scrofulous subjects need not be specially mentioned here. We have already remarked that the *cheesy pneumonia* which is observed frequently in the scrofulous must not be considered as a mere complication, but as an inflammation, the peculiar course of which depends on the same constitutional predisposition as in other scrofulous affections; we only opposed the attempt to consider every cheesy pneumonia as a scrofulous one.

As regards the relation of cheesy pneumonia to other affections of scrofulous subjects, we cannot maintain that it must necessarily develop at a certain advanced stage of the disease. There are many cases of scrofula in which extensive tuberculous affections of the bones and voluminous tuberculous tumors of the lymphatic glands coexist with perfectly healthy lungs. In other cases slight scrofulous affections of the skin and lymphatic glands are followed by pulmonary phthisis at an early stage.

In no case would we consider that most frequent form of pulmonary affections in the scrofulous (cheesy pneumonia, tubercular inflammation) as a *metastatic* process. The seat of scrofulous diseases is evidently determined by the presence of a peculiar vulnerability and weakness of definite organs and systems. These conditions being referable to hereditary transmission, there is nothing surprising in the fact that scrofulous children, descended from phthisical parents, are eminently predisposed to cheesy pneumonia.

Regarding the relation of scrofulous tumors of the glands to tuberculous pneumonia, we grant that co-existence of considerable tumors (especially of the cervical glands) and this pulmonary affection is frequently observed, but a gradual extension of the affection from the glands to the lungs is neither anatomically probable, nor has it ever been demonstrated. Clinical experience rather speaks in favor of a connection between this pulmonary affection and scrofulous bronchitis.

It has been stated repeatedly, and confirmed, among others, by Phillips, that persons presenting scrofulous cicatrices on the neck are rarely attacked by pulmonary phthisis, but this observation does not amount to much, although it seems to be corroborated by the popular belief prevalent in some countries that individuals with scrofulous cicatrices enjoy immunity from phthisis. So far, however, there is no statistical proof for this belief at all, for the number of phthisical subjects with scrofulous cicatrices (according to the author's observations in Dresden, one per cent.) is without value, because the ratio of phthisis to glandular affections, in which breaking of the abscess has not yet taken place, cannot be stated accurately.

The clinical symptoms of scrofulous cheesy pneumonia are not distinct from those of tuberculous pneumonia occurring in non-scrofulous subjects; we refer, therefore, in regard to them, to the corresponding sections of this work. A detailed description of the symptoms of solitary tubercles of the brain, respectively of cheesy encephalitis, or other cheesy degenerations in the scrofulous (in the genito-urinary mucous membrane, the supra-renal capsules, etc.), may likewise be dispensed with.

We will add only a few words in regard to certain *general symptoms*. The *anæmia* of scrofulous subjects we consider, as already stated above, rather as a secondary symptom than a primary cause of the disease.

The view advocated by Rindfleisch, that the scrofulous constitution is based on a misproportion between the quantity of blood and the weight of the body, has a certain probability, anatomically speaking, as it is known that local anæmia is one of the essential causes of cheesy degeneration of the inflammatory products. The observation, frequently made, that healthy plethoric children become scrofulous, and present symptoms of anæmia only after the disease has been fully developed, speaks, however, against this hypothesis. The fact, first pointed out by Balman, that the *number of white blood-cells is increased* in children with scrofulous tumors of the glands, we can also confirm as to the *later* stages of the disease; but as to children presenting the *first symptoms of scrofulosis*, it has been proved in quite a number of cases that in this stage the ratio of colorless and red blood-corpuscles is perfectly normal.

The *fever* occurring in scrofulosis varies very much, according to the seat and extent of the local processes, and the ease with which absorption of the products of inflammation takes place. Very often the increase of temperature appears in the capricious character of *hectic fever*.

The general *impairment of nutrition* in scrofulosis has been mentioned already repeatedly. It becomes most prominent in disease of the mesenteric glands, in extensive suppurations, especially of joints and bones, and finally on development of tuberculous pneumonia.

The appearance of copious deposits of phosphates and oxalate of lime in the urine[1] has formerly been regarded as a sign of disturbed exchange of matter in scrofulosis; this phenomenon, however, was soon recognized as belonging to this disease neither exclusively nor even in the generality of cases.

Complications and Sequelæ.

We have already remarked that we do not regard cheesy pneumonia as a complication of scrofulosis; *general miliary tuberculosis*, however, must be looked upon as such, for we have to take it either for a real metastasis (by the reception into the blood of tuberculous elements capable of development) or an infection caused by matter formed in the primarily tuberculous or cheesy foci. Peculiar circumstances are required for the evolution of general tuberculosis out of the local affection. The majority of cases in which ulcerations, existing for years and accompanied with copious development of tubercles (especially in the bones), have been observed, are not followed by general tuberculosis, and this fact proves either that the conditions for the absorption of the virus are unfavorable at the seats of the primary tuberculous inflammation, or that peculiar conditions must be fulfilled before general tuberculosis can associate itself with the local disease.

The view especially advocated by Buhl, that every cheesy product, whether it be the result of simple inflammation or engendered by tuberculosis, may cause miliary tuberculosis, is liable to the objection that this latter disease is very rare, compared with the large number of cases in which cheesy deposits exist, and is further contradicted by the fact that cheesy products are known to become absorbed without giving rise to miliary tuberculosis.

Another important complication is that peculiar degeneration which is now generally designated by the term *amyloid degeneration*, first used by Virchow. It associates itself almost exclusively with chronic processes of suppuration and ulceration (particularly in bones), and consequently it is not surprising to meet with it frequently in scrofulous subjects. The nature and special cause of this change are still quite obscure, while its anatomical features may be passed over as generally known.

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[1] *Balman* (l. c.); *Beneke*, Der phosphorsaure Kalk in physiol. und therapeutischer Beziehung. Goettingen, 1850.

We cannot explain in any way why it is that in some cases of scrofulous inflammation amyloid degeneration occurs very early, and generally while it is entirely wanting in other very protracted cases in which the local phenomena are identical, just as it happens with the amyloid degeneration occurring in cases of phthisis, syphilis, etc.

The organs first invaded by this change in scrofulosis are the *lymphatic glands*, in which it occurs in two different ways: it may begin, as it does in other organs, first on the internal coat of the vessels (especially of the small arteries), or it may arise in a circumscribed portion of the follicular substance itself. If the lymphatic gland attacked by the degeneration is neither hyperplastic nor tuberculous, its volume is generally only moderately enlarged, and it may be felt, if situated near the surface, as a rather soft tumor of little elasticity. Next in order of frequency are the amyloid degenerations of *spleen*, *liver*,[1] and *kidneys* (generally also the internal coat of the large vessels, especially of the aorta). In fully developed cases considerable enlargement of the two first-named organs may be noticed on palpation, while albumen and cylindrical casts are found in the urine (especially vitreous casts, which, however, in the author's cases, never answered the iodine and sulphuric acid test).

As sequelæ of amyloid degeneration may be mentioned marked emaciation and hydræmia, which leads to general dropsy, especially when the kidneys are involved in the disease. Clinical experience would warrant the belief that the lighter degrees of amyloid degeneration may disappear again completely.

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[1] *Bordeu* has already described anatomical changes in the liver which evidently belong to this affection (liver dry, increased in size, of yellowish white color; contents of gall-bladder colorless). *Budd* (Diseases of the Liver) describes amyloid degeneration of the liver as a specifically scrofulous disease.

Complications which may arise in the case of scrofulous ulcers and abscesses, as of wounds and ulcers from other causes, are the so-called *accidental traumatic diseases*, traumatic diphtheria, gangrene, erysipelas, and the general infections known as septicæmia and pyæmia. It is, however, a surprising fact that pyæmia associates itself, comparatively speaking, rarely with the chronic affections of joints and bones in scrofulous subjects.

That certain disorders remain in cases in which scrofulosis has become completely extinct, may be concluded from what has already been said. Among these may be mentioned the abnormal conditions resulting from severe cases of scrofulous ophthalmia (opacities of the cornea, staphyloma, opacities of the lens, atrophy of the iris), with their consequences as to the faculty of vision; the deafness frequently remaining after scrofulous otitis, the curvature of the spine caused by spondylitis, anchylosis, disturbances resulting from spontaneous dislocation of the hip-joint, and so on.

Diagnosis.

The diagnosis of scrofulous affections does not generally present any difficulties; but we do not know, as already mentioned, any certain sign of a scrofulous constitution, from which the predisposition could be inferred even before the breaking-out of the local phenomena. The supposition that a definite local process rests on a scrofulous basis results partly from facts proving hereditary disposition, partly from the course of the disease and the simultaneous appearance of similar morbid processes in other parts of the body. In the long run the diagnosis cannot remain doubtful, although it may be very difficult to form a definite opinion at a given moment, especially when the bones are first affected, and the question arises whether the case be one of syphilis or of scrofula.

As regards local tuberculosis, we need make no further remark, having already convinced ourselves that at a certain stage of all severe scrofulous affections local tuberculosis sets in almost regularly. The exact time at which the development of tubercles took place cannot be clinically determined with certainty. The presence of tubercles in tumors of the lymphatic glands may be always assumed whenever they show a tendency to remain stationary in a hard, inelastic condition.

Duration, Termination, and Prognosis.

We have already pointed out the chronic character of scrofulosis and its protracted duration for many years, the disappearance of one group of symptoms being soon followed by relapses or fresh attacks in other regions. The disease appears, as we have likewise stated before, most frequently at the age of from five to seven years, and becomes extinct oftener at the time of sexual development than at any other period. Individuals who have suffered during childhood from severe and obstinate forms of scrofulosis attain the best of health about this time, and show no weakness resulting from their previous disorders.

Phillips mentions having frequently seen scrofulous cicatrices in men distinguished by great muscular strength (for example, in prize-fighters).

In other cases, however, phthisis is developed just at the time of puberty, while the other scrofulous affections continue, or after they have disappeared. Pulmonary phthisis is the most frequent cause of death in scrofulosis; next in frequency are, as already mentioned, affections of the bones and joints,[1] with their direct and indirect consequences; and last, general miliary tuberculosis.

We have no reliable data from which we could infer the percentage of mortality from scrofulosis with any degree of certainty. The proportion of mortality from scrofula to the total number of deaths from all causes has already been referred to; it gives, however, no clue to the solution of this question. As many cases of death from scrofula are accounted for under different heads (diseases of the bones, pulmonary phthisis, etc.), we shall always want for complete material, and it will be especially difficult to find out how many individuals die of phthisis after having recovered from scrofulosis.

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[1] According to statistics collected by *Meinel*, which, however, embrace but few children, there died, among 69 individuals affected with tuberculosis of the bones, 20 of dropsy (amyloid degeneration), 14 of tubercular meningitis, 11 of marasmus, 5 of paralysis of the bladder, 8 of anæmia, 3 of pyæmia, and 3 of nephritis.

This circumstance must be taken into account in the interpretation of the statistical data collected by district physician Dr. Koerner for the medical district of Meissen in Saxony. The total number of cases of scrofulosis is surprisingly small, probably because only the cases which came under medical treatment are recorded. Koerner's tables comprise the years 1867–1872,[1] and contain a total number of 58,466 individuals affected with scrofula, of whom 3,184 (or about 4 per cent.) died, and 661 cases of "constitutional scrofulosis" are recorded (or about 1 per cent. of all cases), of whom only 21 (or 3.2 per cent.) died—a much smaller number in proportion to the total mortality than that reported in the above-mentioned Geneva statistics.

On the *prognosis* of scrofulosis nothing can be said that could be relied upon in all cases, as the termination of the disease depends so essentially on the hygienic conditions under which the patient lives, on the obstinacy, the seat, and extent of the disorder. Prognosis is most unfavorable in scrofulous pneumonia and those cases in which the bones are affected. An absolutely unfavorable prognosis must, however, not be made in the latter cases, especially in younger children, even in the most severe forms, as it is shown by experience that affections of the bones of the most extraordinary severity and extent may end in recovery. We have already said that it would be going too far to see in every scrofulous child a candidate for consumption; in this respect also the hygienic circumstances under which the patient in question lives are of the greatest importance. It is probable that the development of pulmonary tuberculosis from scrofulosis is chiefly favored by crowding together in narrow, ill-ventilated rooms. In well-to-do families the transition from scrofulosis to pulmonary phthisis is consequently observed much more rarely than among the poorer classes. On the intimate relation of these diseases enough has been said already; it remains only to point out the frequent occurrence of scrofulosis in countries in which pulmonary phthisis is but rarely found, as in India according to Balman, in the ore-mountains of Saxony according to Ettmueller, etc

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[1] 1. bis 5. Jahresbericht des Med.-Colleg., über das Medicinalwesen des Koenigr. Sachsen. Dresden bei Heinrich.

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Treatment.

So far as scrofulosis is caused by *hereditary predisposition*, we are powerless as to *prophylactic* measures. A prophylaxis beginning "ab ovo" would be very desirable indeed, and physicians have not been wanting who advocated prohibition by the government of all marriages of individuals from whom a scrofulous progeny might be expected with probability. Such a measure is, however, neither capable of execution nor desirable, and all that can possibly be done in this respect is to induce such individuals by instruction not to form matrimonial alliances. This is certainly desirable, but its result will remain illusory. In the formation of matrimonial alliances every other dower is generally much more deliberately weighed than the physical disposition in question, although it is of the greatest importance to the well-being of whole generations.

There remains, therefore, in this respect only the question whether it be possible to prevent the breaking out of scrofula, or at least mitigate its course by careful treatment even in those who are hereditarily predisposed to it. The measures to be taken for this purpose generally coincide with the prophylaxis against scrofulosis in cases in which this hereditary predisposition is wanting. We may even say that these measures are of universal application, as every rational method of physical culture must be based on them. Still it would be wrong to believe that the breaking out of the disease can be prevented with certainty by a judicious regimen. There is unfortunately no lack of experience to prove that, a hereditary predisposition being given, grave forms of scrofulosis may develop themselves in spite of the most careful treatment—exactly the same experience as has been observed in cases of pulmonary phthisis arising from hereditary predisposition.

In the case of all children, but especially of those in whom a dormant hereditary predisposition to disease exists, the mode of feeding them during the first years of life is of the greatest importance. Children of tuberculous or previously scrofulous mothers must not be allowed to be nursed at the maternal breast. The best substitute is a healthy, strong wet-nurse. When this cannot be had, *artificial feeding* must be resorted to, and there is fortunately in our times no lack of attempts to supply substitutes for mother's milk. In large towns feeding on cow's milk is attended with difficulties, and if the possibility, above alluded to, of transmitting tuberculosis to man by the milk of cows affected with pearl disease should be proved, this mode of feeding would have to be looked upon with the greatest mistrust wherever the existence of perfectly healthy live stock could not be demonstrated to full conviction. What form of artificial feeding ought to be selected, whether condensed milk, Nestle's powder, Liebig's soup, or Hartenstein's "leguminose" be preferable, we cannot discuss here in detail. This has been done of late years by a great many writers. On the whole, no universal rule can be given in this respect, as the individual constitution of the child has to be considered, and as a certain method of feeding does not at all agree with one child, while another will thrive on it remarkably well. The results of our own experience may be briefly stated to be in favor of Nestle's "infants' flour," the use of which was but rarely attended with indigestion, while the nutrition of the child improved in the most gratifying manner; condensed milk also furnished in some cases very satisfactory results, in others the large proportion of sugar contained in it seemed to molest the stomach and intestines.

The feeding of children in the first years of life on the diet of adults is a widely-spread abuse which favors the development of scrofulosis. Parents frequently relate with pleasure that their six or nine months old child is already eating of everything that comes on the table. It is hardly necessary to prove that the eating of rye bread and potatoes, the drinking of coffee, lager-beer, etc., in the first years of life, must exert a disturbing influence on the organs of digestion, and produce especially irritation of the intestinal mucous membrane and mesenteric glands.

Even in later years all articles of food which irritate the alimentary canal, and contain too small a quantity of nutritive materials in proportion to their bulk and weight, ought to be avoided. The diet must consist mainly of good milk, easily digested meat, and well-baked bread. We cannot indorse the absolute prohibition of rye bread and potatoes, as we find it impossible to believe in the injurious character of these articles, if they are of good quality and properly prepared. Highly nutritious and at the same time easily digested food is contained in the leguminous grains, especially in the finely divided form in which they are now sold according to Beneke's prescription under the name of "Hartenstein's leguminose." The soup made from this preparation agrees exceedingly well with somewhat older children whose digestion is rather delicate.

For drinking we can best recommend pure water; well fermented light beer is not to be rejected.

The proper regulation of the number and quantity of meals is of no less importance than the selection of their quality. The development of scrofula, under circumstances which leave nothing to be desired as to the quality of food, is certainly in many cases owing to the fact that children are permitted to eat too frequently and too much. Individuals inclining to scrofulosis are often endowed with a voracious appetite, usually showing itself strongest in the demand for coarse and heavy food, and leading only too easily, if indulged too much, to a permanent condition of irritation of the organs of digestion, to which no rest is ever permitted. In this respect we must point out the much practised abuse of presenting children with all sorts of candies, chocolate-drops, etc. As the friends of the family sin much more in this respect than the parents, the exclamation: "The Lord protect them from their friends," would be fully justified.

Of even greater importance almost than proper food is the inhalation of pure air. Frequent exercise in the open air, well ventilated sitting- and bed-rooms are absolutely necessary. Unfortunately the opinion is still prevalent, especially in large towns, where dwelling accommodations are scarce and expensive, that the worst and smallest room is perfectly sufficient for a sleeping apartment. The proper ventilation of school-rooms is especially important in the respect here considered.

As to the hygienic treatment of children in other respects we would draw special attention to the demands of proper *muscular training* and *culture of the skin.* The first, the more important of the two, must be met in towns by a methodical instruction in gymnastics, while in the country the necessary exercise of the muscles comes in as a matter of course. Proper exercise of all the muscles and its beneficent effects on respiration, digestion, and the totality of physiological functions is of such paramount importance that the place recently assigned to gymnastics in the public schools as a part of compulsory education must be approved with the greatest satisfaction. It is advisable also to begin at the earliest possible age with a judicious and methodical instruction of children in the lighter gymnastic exercises (especially calisthenics).

Culture of the skin, especially cold sponging, practised regularly, and begun at a very early age, is likewise of very great importance. Aside from other advantages this practice makes the body less sensitive to external, especially atmospheric influences, and thereby the exciting causes of an outbreak of scrofulous inflammations are diminished in number and force. It is further self-evident that too warm clothing and bedding must be avoided as causes of effemination, as has been pointed out already by Hufeland. It is true that often enough, with all these precautions, scrofulosis cannot be prevented, but much has been attained already if the course of the disease is only mitigated. As far as the condition of the poor is concerned, especially as regards salubrious dwelling and food, these rules will unfortunately hardly ever be followed.

When morbid processes have developed themselves on the basis of the scrofulous constitution the same rules which have just been indicated must be observed as to dietetic treatment in general, subject of course to exceptions in cases of special indications of a more or less nutritious and easily digestible diet, and to the demands of the general condition of the patient, especially the state of his digestive organs.

Attempts have been made also to combat the scrofulous predisposition, or, as many imagined, the scrofulous virus, by quite a host of *medicines.*

Cl. Faure states already that nearly every remedy contained in the materia medica has been tried against scrofulosis.[1] It was frequently believed that a specific had been found, but soon this was replaced by another.

It cannot interest us to name all the remedies which alternately reigned supreme over the therapeutics of scrofulosis; we shall only mention *mercury*, *antimonials*, particularly recommended by Hufeland; *hemlock*, *iodine*, made quite popular for a time by the highly colored communications of Lugol; the *leaves of the European walnut-tree*, represented as a specific by Négrier; *chloride of calcium*, the antiscrofulosum brought again into notice in the most recent time by J. Begbie; *chloride of barium*, *phosphoric acid*, *phosphate of lime*, etc. According to our ideas on the essential nature of scrofulosis we cannot expect that any specific will ever be found, but we have nevertheless to accord a decided importance to medicinal treatment, which ought to be limited, however, to combating the several symptoms of the disease, and not aim at removing its fundamental cause.

We have to speak in this connection of a remedy which is up to the present day used with uncommon frequency in cases of scrofula, and for a long time enjoyed the reputation of a specific; this remedy is *cod-liver oil.*

In England, Holland, and on the northern coast of Germany, cod-liver oil had been used long since as a domestic remedy for obstinate rheumatism and gout. The profession, however, became generally acquainted with it as late as the third decade of this century.[2]

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[1] We need not be astonished at seeing also sympathetic and other remedies based on superstition employed against so obstinate a disease, even in our own days. *Plinius* already speaks of the former, and among the latter we only mention a method of cure, which, however, is no more believed in at the present time, by the laying-on of the king's hand, from which the designation "*the king's evil*" has been derived. This superstition existed already in the time of the Roman emperor Alexander Severus: "Regius est vero signatus morbus hic, quoniam celsa curatur in aula" (Sereni Samon. Poem. LIX.); later the power of healing goitres and glandular tumors by the laying-on of hands was especially ascribed to the kings of France and England (particularly Edward the Confessor), "le roi te touche, le roi te guérit." (Comp. *Choulant*, Cure of Scrofula by the King's Hand, 1847.)

[2] In Germany, especially through *Schuette* (Beob. ueber den Nutzen des Berger Leberthran. Horn's Archiv, 1824. S. 79); in England, through *Percival* (Medic.

Very different views have been expressed on the *modus operandi* of this remedy. According to some it acts as a stimulant to secretion and excretion, but interferes easily with digestion at the same time, while others ascribed to it, on the contrary, a beneficent effect on digestion; most generally, however, its favorable influence on general nutrition was recognized. The active principle was formerly found, under the influence of Lugol's doctrines, in the minute quantity of iodine it contains (Haeser), while later authors assert[1] that cod-liver oil is only to be considered as fatty food.

Attempts were made accordingly to substitute other fats (olive oil, neat's-foot oil, dog's fat, etc.) for cod-liver oil, but it was soon found out that these were not as easily borne by the stomach, and frequently remained without a favorable influence on nutrition. Berthé[2] was led by his clinical experience to the opinion that cod-liver oil acted only through its fatty constituents, but was more easily digested than the common vegetable fatty substances. O. Naumann[3] arrived by his experimental researches to the conclusion that cod liver permeated dry and wet animal membranes more easily than all other fixed oils, and is also more readily oxidized than these. He ascribed these properties of the cod-liver oil to the bile contained in it, the darker varieties being especially rich in this constituent. According to Buchheim's[4] investigations this statement is incorrect—cod-liver oil is distinguished from most other fixed oils by containing free fatty acids, besides the glycerides (about five per cent. in the lighter, and a somewhat higher percentage in the darker varieties).

The greater digestibility of cod-liver oil is attributed by Buchheim to the fact that by the neutralizing action of the alkaline intestinal juice on the free fatty acids contained in it, larger quantities of glycerides are prepared for reception into the blood than could have been taken up under the influence of gall and pancreatic juice alone. *Cod-liver oil* plays the same part in the digestion of fat which is played by Liebig's infants' soup in the digestion of starch: by the use of either of them the intestinal canal is relieved of a portion of its work. On this view Buchheim founds his recommendation to add a certain quantity of fatty acids to cod-liver oil in order to make it still more easily digestible, and to select for this purpose oleic acid as the best. This recommendation is, however, still without practi-

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essays), *Donovan* (Communication on the preparation and med. properties of cod-liver oil. Dublin Journ. Sept. 1844), and *Bennet* (Treatise on the Ol. Jec. Aselli. Edinb. 1848).

[1] *Thompson*, Bull. de Thérap. July, 1851, p. 11.

[2] Gaz. médic. de Paris, 1856. No. 21.

[3] Archiv der Heilkunde. Leipzig, 1865. S. 536.

[4] Arch. f. exp. Pathol. und Pharmak. III. 2. H. S. 118.

cal value, as pure oleic acid cannot be manufactured in sufficient quantity, and the ordinary oleic acid of the shops is unfit for such a use, on account of its disagreeable acrid taste.

Foster recommended to give cod-liver oil with a little ether, because it had been shown by Cl. Bernard that ether increases the secretion of pancreatic juice.

Whatever may be the correct explanation of its *modus operandi*, the excellent effect of cod-liver oil in certain cases has been empirically proved beyond doubt. According to Niemeyer[1] cod-liver oil acts most beneficently in those constitutions which have been described as representatives of the erethic form of scrofulosis. Patients of this class being always poorly nourished, its indication here is apparent, while it is contra-indicated in the fleshy, bloated patients of the torpid class. We would also lay additional stress on the decided efficacy of cod-liver oil in the treatment of scrofulous affections of the bones and scrofulous ulcers. On glandular tumors, however, it seems to produce no effect whatsoever.

Concerning the mode of administering it we would recommend to begin with small doses (about a dessertspoonful twice a day) and to give it always on a full stomach, say half an hour after meals. Experience shows that most patients soon get used to cod-liver oil and look upon it finally as a delicacy. In some cases, however, it is not well borne, and causes nausea, vomiting, and loss of appetite.

Regarding the administration of *iodine* against scrofulous affections, a good condition of nutrition is generally considered as a prerequisite. Long-continued iodine treatment, as recommended by Lugol with so much emphasis, appears to the impartial observer to be entirely useless in most cases. It may perhaps be recommended in grave affections of the bones or of the brain. Iodine is most frequently used combined with iron, especially in the form of syrup of the iodine of iron.

The least dangerous preparation of iodine is doubtlessly the water of the *Adelheid spring, of Heilbronn*, which contains, besides iodide of sodium, relatively considerable quantities of bromide of sodium, and is rather rich in carbonate of soda. This mineral water is always well borne, and numerous witnesses speak favorably of its curative effects in scrofulous affections. Von Nussbaum reports that he has seen cases of the severest scrofulous affections of bones, which were sent to him for amputation, recover under the use of this water.

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[1] Handb. der spec. Path. und Therapie, II. Bd.

The administration of *iron* will be indicated when anæmia of a high degree is present, and then the mildest preparations only ought to be used—lactate of iron, pyrophosphate of iron water, etc.

Among the mineral waters those containing common salt are most frequently used, to which the power of producing a more rapid interchange of the albuminates (increased excretion of urea) has been ascribed.

The usefulness of bathing in the water of common salt springs has been especially proclaimed for cases of glandular tumors, inflammation of the connective tissue, chronic catarrh of the mucous membranes, and affections of the skin. In these cases drinking of the water of such springs is generally recommended with the external use of it, and under certain circumstances increasing the effect of the bath by the addition of mother-lye. Stress has also been laid on the iodine and bromine contained in the water of such springs, especially in the mother-lye of Kreuznach, Oeynhausen, Elmen, Hall, Arnstadt, etc., the effect being ascribed to the inhalation of the vapors emanating from the water. It would be superfluous to enumerate all the salt springs[1] which are more or less fashionable at the present time for the treatment of scrofulosis, but we cannot omit the remark that the leading consideration in recommending this treatment is with us whether or not a particular spring fulfils those hygienic conditions as to purity of air, protection against winds, etc., which are of the greatest importance in such a selection. We will not deny, however, that the methodical use of those baths exerts a beneficent influence on the function of the skin and indirectly also on the entire economy of the body.

Sea-baths have been specially recommended to those suffering from the torpid form of scrofulosis. In the beginning, warm sea-baths have been advised as preferable, but the sojourn on the sea-coast with its bracing air seems to be the principal desideratum. Experience has proved, however, that scrofulous affections of the eye get worse at the sea-side, while affections of the bones and voluminous solid tumors of the glands remain stationary.

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[1] Comp. *Helfft*, Handb. der Balneotherapie. 7. Aufl.

Hydropathic treatment has been advocated by Niemeyer in the torpid form of scrofulosis as a means of accelerating the sluggish change of matter.

In the hands of a fanatical hydropathist this method of treatment will as often prove hurtful as beneficial. If rationally employed its beneficent effect is frequently undeniable. Wrapping up in wet sheets, according to Schroth's directions, is especially to be recommended. The application of the cold douche to scrofulous tumors of the glands has in our experience several times produced a favorable result. Obstinate tumors of this kind, which have resisted all possible salves and plasters, disappear sometimes under the continued application of cold-water epithems.

With regard to all these balneological measures we must not forget that the use of some bath or other for a few weeks can never benefit a scrofulous patient as much as a longer sojourn under favorable climatic conditions. In view of the protracted course of scrofulous affections, and of the deeply-rooted constitutional predisposition, it is hardly necessary to look for a specified demonstration of this assertion. We agree, therefore, fully with Knauthe's[1] advice not to expect everything from a short use of salt-spring baths, but to send scrofulous children rather to some climatic sanitarium for a longer period of time. Unfortunately it is not possible but for the favored few to go to Meran, Nice, Mentone, etc. Considering the great frequency of scrofulosis among the less well-to-do classes it is therefore to be fervently desired that institutions for the climatic treatment of scrofulous children like those already existing in England, France, and Italy should become more general. At Margate, on the coast of England, there is a hospital of this kind with 250 beds; in France the results of the treatment in the hospital at Berck-sur-mer are spoken of in the highest terms.[2] It would be one of the noblest undertakings to establish such institutions in a sufficient number to extend their blessings to all that need them. The places to be selected need not be looked for exclusively on the sea-coast. There are enough favorable situations which might serve as sanataria for scrofulous children, especially those living in large towns. If we consider how heavy a burden a child sick with some chronic complaint (for instance, a spondylitis or some other protracted affection of the bones) is to a family of small means, how much the faculty of the parents to earn a living is paralyzed by the care it requires, we shall be convinced that by establishing such institutions the greatest benefit would be bestowed not only on the suffering children but also on the healthy members of their families. That our ordinary hospitals and even the children's hospitals existing here and there do not generally fulfil those conditions which must be regarded as indispensable for the treatment of scrofulous children, does not require a detailed proof. It is to be hoped that the German nation will soon take the necessary steps for procuring also for the scrofulous children those aids which have been extended already in so satisfactory a manner to the mentally and bodily afflicted of other classes.

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[1] Jahrbuch für Kinderheilkunde. 1873.

[2] Comp. *Bergeron*, Rapport sur les résultats obtenus dans le traitement des enfants scrofuleux à l'hôpital de Berck-sur-mer. Paris, 1866. *Rodolfi*, Trattam. maritim. in S. Ilaria di Nervi, etc., Gaz. med. ital. 1868, November. *S. Engelsted*, Om Nytten of Kysthospitaler til Behandlung of scrophuloese Boern (Ugeskrift f. Laeger III. Bd. XIV.).

Without a judicious general treatment, which, as may be expected from the obstinate character of the disease, requires patience and perseverance on the part both of physician and of parents, the *local treatment* of the several scrofulous affections will also remain without good results. On the other hand, proper care in the treatment of the local affections is of the greatest importance. If we succeed in curing the affections of the skin and mucous membranes we remove one of the most frequent causes of present and future trouble in the lymphatic glands. If we can shorten the processes of suppuration and ulceration we at the same time lessen the danger of grave general disturbances (for instance, amyloid degeneration) setting in.

The principles, from which the topical treatment of the local scrofulous affections has to start, do not differ from those generally accepted in reference to local diseases of other origin. We shall therefore make only a few short remarks without going into details.

Regarding the scrofulous *affections of the skin*, simple cleanliness generally suffices for their treatment. In cases of *eczema*, the scabs ought to be removed (by softening them with olive or cod-liver oil, which is preferred by some). In very obstinate cases cauterization with nitrate of silver, inunction with white precipitate ointment, etc., may be employed.

In *lichen scrofulosorum*, Hebra saw good results from the local as well as general use of cod-liver oil.

In *scrofulous coryza* the injection of cold water or mild astringents, by means of Weber's nasal douche, is indicated.

Scrofulous ophthalmia must be treated with the greatest care. Referring the reader for details to the text-books on diseases of the eye, we will only state that the use of astringent collyria produces very little good effect, that cold-water epithems, which are still generally used in this complaint, are not to be recommended, while ablutions with, or epithems of, lukewarm water are much better. It is probably fortunate for the patient that the cold epithems prescribed by the physician are generally applied in such a manner that they act like warm ones.

Tying up the eyes with heavy materials must be strictly prohibited. Against the great intolerance of light, associated with spasm of the lids, immersion of the face in cold water is a very good remedy, the effect of which, however, does not last longer than a couple of hours. Epithems of acetate of lead with tincture of opium may be used in addition. The indications for instillations of atropine and the surgical operations required by the sequelæ of scrofulous affections of the eye must be omitted here; the application of calomel to the conjunctiva in herpetic eruptions and of white precipitate ointment in blepharitis may, however, be briefly mentioned.

The treatment of scrofulous *affections of the ear* does not require a special discussion; its results are almost always discouraging when the more deep-seated parts are affected.

The *catarrhal affections of the respiratory and intestinal mucous membrane* deserve special attention. By an early treatment of scrofulous bronchitis the setting-in of tuberculous disease of the lungs may be certainly prevented in many cases as well as tuberculosis of the mesenteric glands by properly attending to the digestive function. In reference to the treatment of these catarrhal affections the generally known rules must be observed.

The function of the intestine will be aided best by a proper diet. Mild cathartics (especially rhubarb) are very useful when constipation is present; doing too much in this respect, formerly a very frequent practice, must be carefully guarded against. Long-continued use of mildly astringent beverages (infusion of walnut leaves, acorn coffee) is not to be rejected, but such articles must not be looked upon as specifics, and the all-important general treatment forgotten over their illusory virtues.

Glandular tumors, in which cheesy degeneration has already set in, prove very obstinate to local treatment. We have already mentioned the good effect sometimes produced by the cold douche and cold epithems, but these are seen almost exclusively in the earlier stages of the swelling. The irritating ointments and plasters which have been recommended in great number, and tincture of iodine (best in combination with tincture of galls) act only by bringing about earlier softening and breaking; the same must be said of injections of solutions of iodine into the gland or the parts surrounding it.

Lately *extirpation of the scrofulous gland tumors* has been recommended on the ground that thereby not only radical removal of the local affection is secured, but also the danger of general tuberculosis prevented. To this argument may be opposed the fact proved by experience that local tuberculosis often exists in the body for years without producing any sign of general tuberculosis. Pulmonary phthisis which appears so frequently in scrofulous subjects cannot be regarded in the generality of cases as pulmonary tuberculosis caused by metastasis from the scrofulous glands, but as a sequel to primary pneumonia or bronchitis. If subjects affected with scrofulous gland tumors are predisposed to phthisis pulmonalis, we find the disease of the lungs almost always beginning its development simultaneously with that of the cheesy gland tumors. And experience really shows us that such patients die of pulmonary phthisis some time after, and in spite of, the extirpation of the scrofulous glands. If, however, the danger of general tuberculous infection of the body from the local deposits is principally insisted on, we may ask the question, whether the danger from development of general miliary tuberculosis is greater than that arising from the extirpation of voluminous gland tumors. The answer is doubtful, even if we admit that the danger of such operations diminishes with the increasing experience and care of the surgeon. We have also to consider that in many cases it is not possible to remove all tuberculous matter, which is not only contained in the large cheesy glands, but generally also in those hardly enlarged ones which to the unarmed eye appear still in a healthy condition, and these are frequently so situated that they are quite inaccessible to the operator (the deep cervical and mediastinal glands).

From all these considerations we would not found too great expectations on the use of "iron in the form of the scalpel," so warmly recommended by Hueter as a prophylactic against tuberculosis. The saying of Celsus remains true even in our own time: "Strumæ vel præcipue medicos fatigare solent. Et sive *ferro*, sive medicamento curentur, plerumque iterum circa cicatrices ipsas resurgunt."

As to the local treatment of scrofulous ulcers and diseases of bones and joints we must refer the reader to the text-books on surgery; repeating again the remark that the general conditions in which the patient is placed are of essential importance. In hospitals these cases will often take a less favorable course in the hands of the most celebrated surgeons and with the most careful nursing than in the healthy atmosphere of the country with comparatively simple care. The best will be done when the aid of an expert can be attained under the most favorable hygienic conditions.

With regard to these cases also we have to repeat the demand that special sanitaria for the scrofulous (or generally for chronic diseases of children) may be established in proper localities.

AL SOCIETY

Idiopathic Adenitis.

We shall not discuss, from reasons already mentioned, the secondary and chronic adenitis which associates itself with various infections and simple inflammatory processes. There is left, therefore, only one form of inflammation of the lymphatic glands, that which arises without such a cause as an idiopathic affection, at least apparently so; and as this so-called *rheumatic bubo* is of little importance, we shall dismiss it with a few remarks.

In otherwise perfectly healthy individuals there appears without discoverable cause a lymphadenitis, most frequently in the inguinal and axillary glands, which often terminates in suppuration. In some cases excessive exertion of the corresponding limbs is stated as the cause; for instance, a fatiguing march is followed now and then by inflammation of the inguinal glands and slight, rapidly disappearing swellings are quite a common occurrence after such marches. We may suppose this inflammation to be caused by irritating products of excessive muscular action being conducted through the lymphatic vessels to the corresponding glands.

The course of such inflammations is an acute one, accompanied with slight, general febrile reaction, and always mild. The treatment consists in general rest and the application of emollient poultices adapted to the circumstances; if fluctuation shows itself, artificial opening of the abscess is indicated.

From syphilitic bubo this simple lymphadenitis is distinguished by the absence of primary sores and the rapid healing after evacuation of the matter.

Besides this acute adenitis which ends either in rapid resolution or in suppuration, there occur more chronic swellings of the lymphatic glands, which sometimes may be referred to a continued peripheral irritation (for example, by carious teeth), while in other cases no such exciting cause can be found. The nature of these swellings consists in a simple hyperplasia of the lymphatic glands attaining only a moderate degree, with thickening of the reticulum, in consequence of which the gland assumes a firmer, more fibrous consistence (indurated adenitis). They may remain stationary for a time before they disappear again; in other cases, however, these seemingly insignificant swellings lead to the development of progressive lymphoma, which will be the subject of the following section.

The so-called *granular* lymphoma, which formerly was classified with this affection, has been recognized, as already mentioned, by Schueppel as of a tuberculous nature, and must therefore be separated from it.

MALIGNANT LYMPHOMA (LYMPHOSARCOMA).

Literature.

Hodgkin, On some morbid appearances of the absorbent glands and spleen. Medico-chirurgic. Transact. Bd. XVII. p. 68. 1832.—*Markham*, Path. Transact. IV. p. 177, 1853.—*Bonfils*, Réflexions sur un cas d'hypertrophie ganglion. générale. Soc. méd. de Paris. 1856; Arch. générales. 1865. II.—*Wilks* (*Hodgkin's disease—anæmia lymphatica*), Guy's Hospit. Rep. 3. ser., vol. II. 1856, vol. V. p. 115; Pathol. Transact. XIII. p. 227.—*Wunderlich* (*progressive multiple Lymphdrüsenhypertrophie*), Arch. f. physiol. Heilk. 1858. S. 123; 1866. S. 531.—*Lambl*, Mitth. aus dem Franz-Josef-Kinderhospital in Prag. I. S. 243.—*Hillman*, Pathol. Transact. X. p. 248. 1860.—*Ogle*, Ibidem, XI. p. 255.—*Potain*, Bullet. de la soc. anat. 1861. p. 217.—*Perrin*, Ibid. p. 247.—*Hallé*, Ibid. p. 235. 1862.—*Cossy*, Gaz. hebdomad. 1861.—*Hutchinson*, Pathol. Transact. XII. p. 230. 1861.—*Billroth* (*malignes Lymphom*), Virch. Arch. XVIII. S. 92; ebendas. XXIII. S. 477. 1862; *v. Langenbeck's* Archiv VIII. S. 171; Wien med. Wochenschr. 1871.—*Hillier*, Pathol. Transact. XIII. 1862.—*Barwell* and *Williams*, Ibid. p. 219.—*Virchow* (*Lymphosarcom*), Die krankhaften Geschwülste. Bd. II. S. 728. 1864–1865.—*Trousseau* (*Adénie*), Clin méd. III. p. 555. 1865.—*Hérard*, Archives générales. 1865. II.—*Stromeyer*, Handb. d. Chirurgie Bd. II. S. 408.—*Cohnheim* (*Pseudoleukämie*), Virch. Arch. XXXIII. S. 452. 1865.—*Payne*, Pathol. Transact. XIX. p. 401. 1868.—*Murchison*, Ibid. XX. p. 192.—*Moxon*, Ibid. XX. p. 480. 1869.—*Ollivier* et *Ranvier*, Gaz. méd. 1868. No. 27.—*Eberth*, Virch. Arch. XLIX. S. 63. 1870.—*Arnés*, Presse méd. belge. 1870. No. 8.—*Picot*, Gaz. des hôpit. 1870. No. 116.—*Dickinson*, Path. Transact. XXI. p. 368. 1870.—*Turner*, St. Barthol. Hosp. Rep. VI. p. 117.—*Hüttenbrenner*, Jahrb. für Kinderheilkunde. 1871. S. 157.—*Langhans* (*malignes Lymphosarkom*), Virch. Arch. LIV. S. 509. 1872.—*Hesseling*, Nederl. Tijdschr. 1872. No. 42.—*Lannelongue*, Gaz. des hôpit. 1872. No. 41.—*Panas*, Ibid. No. 116.—*Trélat*, Ibid. No. 57.—*Lücke*, Pitha-Billr. Lehrb. d. Chirurgie. Bd. I. 1. Abth. (Geschwülste); Deutsche Zeitschr. f. klin. Chirurgie. II. S. 238.—*R. Mayer*, Arch. d. Heilk. 1871. S. 154.—*R. Schulz* (*Desmoidcarcinom*), Arch. d. Heilk. 1874. S. 193.—*Czerny* und *Tholen*, v. Langenbeck's Archiv XVII. Bd. 1. H. 1874.—*Winiwarter*, Ibid. XVIII. Bd. 1. H. 1875.

Introductory and Historical Remarks.

The apparently idiopathic affections of the lymphatic glands to be treated of in this section were formerly classified, partly with the carcinomatous tumors, partly with the malignant forms of scrofula. They differ from the scrofulous affections of glands, especially by their small tendency to the production of cheesy masses (respectively to the development of local tuberculosis), and by their pernicious course which puts them on a level with the most malignant tumors.

The nomenclature of these affections is still in a rather unsettled condition. *Hodgkin's disease*, *progressive glandular hypertrophy*, *adenia*, *pseudoleukhæmia*, were used as comprehensive terms for these tumors of the lymphatic glands; in the most recent time, however, they are most frequently designated as *malignant lymphoma* (Billroth) and *lymphosarcoma* (Virchow).

The last designation may give rise to mistakes, inasmuch as it is also used for sarcomatous tumors in general, the structure of which resembles the type of a lymphatic gland, even when they occur primarily in other organs. On the other hand, sarcomatous tumors of the ordinary structure of this class occur in the lymphatic glands, and in the first stage of our disease we have to deal also principally with an essential hyperplastic process. We shall say more on this point later on, and content ourselves now with having justified the selection of Billroth's designation, which is sufficiently characteristic in an anatomical as well as clinical sense. The name "*pseudoleukhæmia*" suggests, it is true, the close relation between leukhæmia and this affection, but it is very inappropriate in all other respects.

As lymphoma shows a very close resemblance with other external tumors in its clinical course it might seem that it belongs mainly to the domain of surgery. Experience has taught, however, that, in the majority of cases, it had to be treated by the physician, and we are thereby justified in treating of it in a work devoted to internal diseases. We may at the same time mention that, in regard to this affection, medicinal treatment can boast of considerably better results than surgical interference.

From the above bibliographical synopsis it may be seen that Hodgkin was the first to draw attention to the morbid processes in question as a separate form of disease; cases of different nature are, however, jumbled together in his description of it. Not before Virchow had described leukhæmia, and its relation to tumors of the lymphatic apparatus, was it possible to accumulate a number of cases which could with certainty be claimed as belonging to our disease and which excited great interest mainly by presenting the same anatomical features as leukhæmia, while it differed from the latter by the want of a corresponding change in the blood.

On looking through the older records there is no lack of cases which may be assigned to this class with great probability; we will refer in this respect to the writings of Morgagni,[1] who relates observations of Aëtius, Wharton, Laub, and others, similar to his own.

The literature of recent times is relatively rich in observations of cases belonging to our disease. There is considerable divergence as to its proper designation and pathological position, but as to the detailed description of the several cases there is evident agreement. It would lead us too far into details if we would report the observations of the several writers; we shall, therefore, simply state that Wunderlich made the first accurate clinical reports on the course of this disease, while Virchow assigned to it its proper pathological position. The first prospect of a successful treatment was opened by the experience of Billroth, whose histological researches in this field also deserve great credit. In the above quoted writings of Virchow, Wunderlich, Langhans, and R. Schulz, an exhaustive digest of the histories of cases so far known may be found.

Etiology.

The causes of the formation of progressive lymphoma are as yet totally obscure. Only in isolated cases the first development takes place in lymphatic glands already swollen in consequence of some irritative process. Between *scrofulosis* and malignant lymphoma there seems to be no relation of cause and effect, and in many cases the absence of the scrofulous habit is expressly noticed. There is likewise no definite evidence of any connection with *syphilis*, if we except one of Hodgkin's cases, in which syphilitic hepatitis was present at the same time. In one of Wunderlich's cases E. Wagner declared the tumors, after having examined them anatomically, as syphiloma, but the history of the case furnished no ground for suspecting any hereditary or acquired syphilitic taint of the child.

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[1] De sedibus et causis morborum. Lib. V. Epist. LXVIII. Art. 12 and 14.

In four of the reported cases the patients had previously had intermittent fever, in two the tumors began to develop after an attack of whooping-cough, and in one after child-bed. In several cases the patients were addicted to drinking, while in others violent emotional excitement had preceded the swelling of the glands. The great variety of the antecedents and the circumstance that, in the majority of observed cases, no cause whatever could be found, furnish sufficient proof that the etiology of malignant lymphoma is still totally unknown.

The disease has so far been observed more frequently in the male than in the female sex, the majority of cases occurring between the ages of twenty-five and thirty-five years; among children (from the fifth to the twelfth year) malignant lymphoma was also found rather frequently. Some cases have been observed, however, at a more advanced age: by Wunderlich, in a laborer of fifty-six, by Billroth in a woman of forty, by Ollivier and Ranvier, in a woman of fifty-nine years of age, etc. The author can add to these the case of a man aged seventy-two that came under his own observation.

Pathology.

Course of the Disease.

Malignant lymphoma is so closely allied to the lymphatic form of leukhæmia, in its clinical course and anatomical features, that it has been proposed by Langhans to combine at least the *soft* variety of lymphosarcoma with the leukhæmic formation of lymphoma, and to designate them with the term *adenia*, introduced by Trousseau. Considering the common features of these diseases, we cannot avoid the question, Why is it that the change of blood does not show itself equally in both? The explanation suggested by Cohnheim, in reference to his case, that the occurrence of the leukhæmic change in the blood has been prevented, perhaps, by the short duration of the disease, falls to the ground, because quite a number of cases have been observed in which no alteration of blood took place, although the lymphomata had existed for years. We might ascribe this difference to a different condition of the lymphatic channels (occlusion of them in malignant lymphoma), but sufficient anatomical investigations are still wanting to warrant such a conclusion. In some cases, it is true, attempts to inject the swollen lymphatic glands artificially have been made with a negative result, but such attempts remain unsuccessful also in some cases of leukhæmic glandular tumors.

The possibility that the two diseases are different in nature, although similar in some of their features, cannot, however, be excluded as yet.

Two forms of malignant lymphoma (or lymphosarcoma) have been distinguished—a *hard* and a *soft* one. This division, first pointed out by Virchow, is essentially based on anatomical differences in the behavior of these tumors. Langhans also urges this distinction, mainly on anatomical grounds; but he lays especial stress on the fact that, as yet, we are only acquainted with a purely lymphatic and a mixed lienal-lymphatic form of the hard lymphosarcoma, while no purely lienal variety has been found, as in leukhæmia and soft lymphosarcoma. Excluding the consistence of the tumors, no differences are observed in the clinical course of the two forms; it might be supposed that hard lymphoma must be distinguished from the soft by a slower course and less tendency to metastatic formations, but this supposition, probable as it appears *à priori*, is entirely unsupported by empirical evidence.

Langhans himself acknowledges, however, that this distinction of a hard and soft form is not well defined; tumors are actually found standing between the two extremes, and in the same individual harder and softer tumors are also observed at the same time.

The disease begins, as a rule, without any prodromata, as an apparently local affection in form of a moderate painless swelling of one or more lymphatic glands, the glands of one side of the neck beginning to swell first in the majority of cases. In this stage it is impossible to find out whether the case be one of benign hyperplasia or malignant lymphoma. As Billroth correctly observes, it can never be said in the beginning of a glandular swelling how it will turn out. Later on, more glands become involved in the process of enlargement, regular chains begin to form, and finally voluminous bunches, consisting of several swollen glands. They may extend, for instance, on one side of the neck from the angle of the jaw down to the clavicle. At this period the general health of the patient is mostly totally free from disturbance; the growth of the tumors takes place sometimes gradually, sometimes in sudden starts. Later still, swelling of the lymphatic glands in the most diverse regions of the body is superadded. And this does not proceed regularly in the order of anatomical continuity, for it is no rare occurrence that the development of tumors on one side of the neck is followed by swelling of the axillary glands of the opposite side, and then of the inguinal glands, and so on. Finally, almost all the lymphatic glands of the body may swell and form voluminous bunches, and when this process once affects the whole lymphatic apparatus, sometimes even before, we find also enlargement of the spleen.

As soon as all the lymphatic glands become involved in the disease, the *general health* begins to suffer, and extreme emaciation, with gradually increasing *anæmia*, follows.

According to the situation of the affected lymphatic glands, and to the degree which the disease has reached, its physiognomy is subject to certain modifications. Sometimes symptoms appear at an early stage which must be referred to disturbance of the respiratory organs by glandular tumors within the thorax, and in these cases death may result at a time when the patients are not yet much reduced; in others death occurs suddenly, under the symptoms of paralysis of the heart. Tumors of the portal glands may, in similar manner, produce ascites at a very early period.

When death does not occur under the influence of a local affection of this kind, and extraordinary development, or by the appearance of some grave complication, cachexia of the severest degree ensues. The anæmia becomes so prominent that Wilks named the disease after this symptom *anæmia lymphatica.* As this anæmia, however, like the anæmia of scrofulosis, must be considered, not as the cause of the disease, but as the consequence of local affections of the lymphatic apparatus, the above designation is not appropriate, although the symptom from which it is taken is one of the most prominent.

In the last period of the disease insomnia is a frequent symptom (sometimes, on the contrary, somnolence is present), the appetite is completely lost, profuse diarrhœa sets in almost without exception, dropsical symptoms appear, bed-sores form, and finally the patient sinks into collapse.

Anatomical Changes.

We have already stated that a soft and a hard form of lymphoma are distinguished which sometimes may be found simultaneously in the same patient.

The *soft tumors* are of an almost fluctuating consistence, and present, on section, a grayish red or white medullary surface, dotted frequently with hemorrhagic specks. The several glands composing the cluster of tumors may still be clearly distinguished; they are connected by loose connective tissue, and the skin is not adherent, as a rule, to the tumors, but unchanged and freely movable. Cases in which the skin becomes consolidated with the tumors must be explained by inflammatory processes in the surrounding parts almost always caused by irritating local treatment

Only in rare instances the neoplasm breaks through the capsules of the glands, and invades the neighboring tissues in its proliferating growth.

On *microscopical* examination we find great increase in the number and size of lymph-cells, several kinds of nuclei, and transitions from nuclei surrounded by a scanty layer of protoplasma to larger formations, all of which phenomena suggest that a lively process of cell division has been going on in the diseased glands. The septa of the gland are almost split up into single fibres by the active cell proliferation. The reticulum is also covered up by cells, and only to be recognized on sections from which these cells have been brushed away with a pencil. The lymph channels within the gland have become indistinct, and the border between cortical and medullary substance completely abolished. The capsule is very rarely perforated by the neoplasm, as already mentioned, but its tissue is always infiltrated with spheroidal cells. In the lymphatic vessels which enter and leave the gland no remarkable change has been discovered so far.

This change in the lymphatic glands may therefore be characterized as a *highly developed hyperplastic cell-proliferation.*

The *hard lymphoma* is distinguished by a firm consistence. While from the cut surface of the soft variety there oozes a milky juice, the section of the hard is dry, of a pale yellow color, and frequently of almost fibrous appearance. As to bulk the hard lymphoma does not equal the soft, and rarely exceeds the size of a hen's egg.

The essential features of the microscopical appearance are thickening of the capsule, septa, and reticular trabeculæ; sometimes sclerosed portions are found, consisting of very dense connective tissue; in other places rather numerous cells, often with many nuclei (even giant cells), are deposited between the broadened trabeculæ of the net-work; and now and then we meet in the same gland, by the side of more fibrous portions, with some that resemble exactly the appearance presented by soft lymphoma. The lymphatic channels are here also distinguishable, and the walls of the vessels are very much thickened. Periadenitis is rare also in the hard variety of lymphoma.

We see that there is no essential contrast between the microscopical appearances of the hard and the soft variety; in the latter, cell-formation is more abundant, and the new-formed tissue preserves mainly the embryonic character, while in the hard form the new-growth undergoes a species of fibrous metamorphosis. The correctness of this view is best demonstrated by the occurrence of transitions from one form into the other, and sometimes this transformation of a soft gland into a hard lymphoma can be actually observed during the course of the disease.

Regressive metamorphosis does not take place, as a rule, in either variety, and cheesy deposits have been found but rarely in the glands so enlarged. In a few cases extensive *amyloid degeneration* has been discovered in the lymphatic glands and in other organs. Pretty frequently fatty degeneration appears to a moderate extent in the cells of the new-growth.

Changes similar to those going on in the lymphatic glands are found in the remaining lymphatic organs, but they generally impress us as being only secondary results of the disease.

The *spleen* especially is almost without exception altered in appearance, generally considerably increased in size, sometimes firm, sometimes soft in consistence (and this without any parallel relation to the hard or soft form of the swellings of the lymphatic glands). The Malpighian corpuscles are considerably swollen, sometimes appearing as grayish yellow nodes of the size of a filbert, standing out in bold relief from the mostly brownish red ground of the pulp, and giving a peculiarly vivid appearance to the cut surface of the organ.

Of other lymphatic organs the follicles at the base of the tongue and *the tonsils* sometimes participate in the disease; the latter may even be the starting-point of the development of lymphoma.

Another interesting fact is the occurrence of changes similar o those found in leukhæmia, in the *follicles of the intestinal mucous membrane;* a series of cases in which these changes have been observed are communicated by Wunderlich, Cossy, and Eberth, to which the author is able to add the following:

A lady aged twenty-eight, having always previously enjoyed good health, and never suffered from any scrofulous or syphilitic affection—the genitals being in a virginal state—had noticed about a year ago gradually increasing swelling of the lymphatic glands on the left side of her neck, which finally formed several clusters larger than a man's fist, and extending from the angle of the jaw to the clavicle. Later on, the glands of both axillæ became also swelled. All these glandular tumors were rather soft, and the skin over them mobile. Of the remaining symptoms only the following deserve to be mentioned: The patient became gradually anæmic to a great degree, but examination of the blood did not show any increase in the number of white blood-corpuscles; swelling of the spleen was discovered about six months after the beginning of the disease; during the last month pleuritic exudation on the left side, moderate ascites and œdema of the lower extremities set in, and finally death ensued under symptoms of collapse. During the last period thin evacuations became frequent, not amounting, however, to profuse diarrhœa.

The *autopsy* disclosed swelling of almost all the abdominal and to a lesser degree also of the mediastinal glands, besides that of the external lymphatic glands already mentioned. They were all found somewhat softened, their condition answering, on microscopical examination, the description given above of soft lymphoma. The spleen was considerably enlarged (weight 750 grammes), and harder, its Malpighian bodies raised in the form of pale yellow nodes attaining the size of a lentil, the pulp of a brownish red color. In the four inferior loops of the small intestines (more thinly distributed also in its superior portion) *the agminated and solitary follicles rose from the surface in smooth, dull white, sharply-defined stratiform masses of the size of a silver dollar*, showing, however, no traces of ulceration. In some of the patches the new-growth had evidently passed beyond their original peripheral limits, the medullary masses forming here and there semicircles on the internal intestinal surface, while in other places the cell-infiltration had extended down to the serous coat. The microscopical appearance of the swollen portions resembled that of the lymphatic glands. The mesenteric glands were considerably enlarged. Among the other anatomical changes we may mention the considerable increase of the bulk of the *liver*, and the presence on the *left pleura costalis* of a number of flat, dull-white new growths, about the size of a dime, resembling in structure the tissue of lymphatic glands. In the other organs no metastatic nodes were found. As no mention is made in most reports of similar cases of the condition of the bone-marrow, we will state that in our case the marrow of the ribs, vertebræ, and cranial bones was found normal. The blood of the corpse showed no increase in the number of white blood-corpuscles.

Changes of the *bone-marrow*, which, according to recent investigations, participate so frequently in leukhæmic disease, have been reported only in one case by R. Schulz, who found in the marrow of the ribs, vertebræ, and sternum peculiar gelatinous deposits of a reddish yellow color.

So far we have described only changes in the lymphatic apparatus, but in numerous cases tumors have been discovered in *other organs* also, which must be considered as analogous to the metastatic localizations of malignant tumors.

They occur in the form of nodes from the size of a millet-seed to that of a walnut, and were most frequently found in the *liver* (following the ramifications of the portal vessels) and in the *kidneys*, more rarely in the *lungs* and *serous membranes*, and most rarely in the *ovaries*, *testicles*, and the *brain*.

The nature of these metastatic deposits is similar to that of lymphoma. Among them also we find two varieties, soft nodes of lymphoid structure, and hard ones of a more fibrous character.

Regarding other changes, we have to mention that the *liver* was considerably enlarged in the majority of cases and that diffuse proliferation of the periportal connective tissue was found in it aside from the metastatic nodes.

In several cases diffuse cell-proliferation was observed in the connective tissue of the *parotid gland* and *pancreas* at the expense of the glandular parenchyma of these organs.

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Symptomatology.

After all that has been said on the general course of the disease and the anatomical changes caused by it, only a few of the symptomatic phenomena will require a special description.

The disease commences, as already stated, with swelling of the cervical, more rarely of the axillary or inguinal glands, although cases have been observed in which the internal glands were the first or exclusive seat of the disease. In such cases the nature of the disease will remain totally obscure as long as the tumors are not accessible to palpation.

The history of a case of this kind, which is also interesting in an etiological point of view, may be given here in brief.

A married woman, aged twenty-six, was taken with the symptoms of typhoid fever. Her case was observed in the City Hospital of Dresden, division of S. Med. Counc., Dr. Fiedler, and with regard to temperature, pulse, evacuations, roseolar eruption, etc., resembled a moderately severe case of enteric fever so completely that the correctness of the diagnosis was never considered doubtful in the least. In the fifth week temperature and pulse came down to the normal standard, and the beginning of convalescence was confidently expected, when the patient, to her attendant's astonishment, began to emaciate more and more, and became anæmic in a higher and higher degree, without any assignable special cause. Sleep became disturbed, appetite ceased, and evacuations, which heretofore had been tolerably normal, assumed the character of diarrhœa towards the end. Temperature remained normal four weeks after cessation of the febrile symptoms, but afterwards it began to rise every evening, becoming normal again in the morning. Finally, œdema of the lower extremities appeared and the patient died in a state of great exhaustion in the sixth week after the disappearance of the typhoid symptoms.

The autopsy showed unmistakable *evidences of typhoid fever* in the ileum (patches dotted with pigment and pigmented cicatrices), but no recent swelling of the follicles. The *mesenteric glands* of the entire ileum were swollen, some to the size of a filbert, others to that of a hen's egg, rather hard, of a homogeneous grayish white surface on section, and without a trace of cheesy deposit. These glandular swellings extended as far as the root of the mesentery; the portal and retroperitoneal glands were swollen to about double their normal bulk. Microscopic examination revealed no tubercles in the lymphatic glands, but thickening of the septa and reticulum, with numerous large and frequently multi-nucleated lymph-cells in the gaps. The *spleen* was considerably enlarged, its weight 850 grammes, the Malpighian corpuscles distinctly visible, of grayish white color, the stroma abundant, the pulp pale. No amyloid reaction in the spleen or lymphatic glands. The scanty wine-red blood showed no essential increase in the number of white corpuscles. In the other organs nothing abnormal was found aside from their anæmic condition.

We cannot assign to this case any other position but that of malignant lymphoma. Its peculiarity consists only in the circumstance that the formation of the tumors immediately succeeded the typhoid swelling of the glands, and this would almost justify us in calling it a typhoid lymphoma which had assumed a progressive character instead of the regular resolution.

Aside from its relation to the typhoid fever, which must explain the rapid termination in death, this case resembles in some respects the one reported by R. Maier (l. c.) in which the disease also originated in the mesenteric glands and presented likewise the hard form of lymphoma.

The peculiar character which may be impressed on the disease by voluminous swellings of the *bronchial glands* has already been mentioned. Violent bronchitis, disturbances of the return current in the descending vena cava, and, above all, extreme dyspnœa must be specially mentioned. The dyspnœa sometimes amounts to the highest degree of orthopnœa. The author has seen a patient of this class who was obliged for weeks to sit up in bed, inclining the head and shoulders forward because he could get some ease only by assuming this position. In his case, as the post-mortem examination proved afterward, the mediastinal and bronchial glands were enlarged to enormous tumors which compressed the bronchi mainly from before backward.

If the tumors are situated very high up in the neck, and especially if the tonsils participate in the new growth, difficult deglutition, impeded vocalization, etc., may occur at an early period.

It has also been mentioned already that the tumors may assist in causing dropsical symptoms, especially ascites, by impeding the circulation of the lymph and blood.

We cannot as yet decide the question whether the *palpitations of the heart* repeatedly observed in these cases, the *fre-*

quent and small pulse, even when no fever is present, and the fatal termination sometimes caused by *paralysis of the heart*, are owing to the pressure exerted by the tumors on the nervous apparatus (pneumogastric or sympathetic), or whether the disturbances in the functions of the heart are rather due to the extreme anæmia. In several cases it is expressly stated that important nervous tracts have been interfered with by the tumors. Ollivier and Ranvier relate that in their case the pneumogastric and recurrent laryngeal nerves were included in a cluster of glands weighing 700 grammes. In other cases, again, the heart was found in an atrophied condition after death, and sometimes fatty degeneration was present.

Of other symptoms caused by lymphoma in certain regions, *icterus* must be mentioned, which sometimes occurs, and then must be ascribed to compression of the biliary ducts by swollen portal glands (or metastatic tumors of the liver).

The profuse diarrhœa which generally comes on toward the end must not be ascribed to the local affection of the intestine, as has been done by Wunderlich, for it occurs also in those cases in which no such change of the intestinal lymph-follicles is found after death.

A frequent symptom, mostly associated with *considerable enlargement of the spleen*, is a sense of fullness in the abdomen; violent and long-continued abdominal pains, radiating along the back and the lower extremities, are also often felt.

The appearance of *albumen in the urine*, when the disease is seated in the *kidneys* (tumors, sometimes complicated with diffuse degeneration), may also be mentioned *passim*.

The *temperature* of the body does not present any characteristic change in cases of malignant lymphoma. In the earlier stages there is generally no fever; later on an increase of temperature is often found in the evening, which returns to the normal standard, sometimes even falls below it, in the morning; towards the end the temperature often sinks below the normal degrees when other symptoms of collapse appear.

Murchison reports a case which in this respect is unique. In a girl, aged six, the swelling of the cervical, axillary, and inguinal glands was ushered in by a fever of ten days' duration, and this phenomenon repeated itself several times after periods of apyrexia lasting about a month.

Among the other general symptoms are extreme *anæmia*, and, running parallel with it, rapidly increasing *emaciation* and *muscular prostration*, all of which are sufficiently explained by the extensive disease of organs so important to the elaboration of blood. The *delirium* (in children *convulsions*) and *comatose condition*, which make their appearance towards the end, are also explained by the reaction of general anæmia on the central nervous apparatus. The tendency to *profuse hemorrhages* from the nose and mouth, and the appearance of *petechiæ* on the skin before death, give evidence of the commencing *dissolution of the blood* (or, perhaps, of the general disturbances of nutrition in the vessels). The frequent occurrence of *bed-sores* has been mentioned already.

In women the disease is, in its earliest stage, often accompanied by metrorrhagia, while later on the menses cease entirely.

Complications.

Amyloid degeneration of the lymphatic glands and other organs has been mentioned as one of the complications of malignant lymphoma, in describing its anatomical features; so has *pleuritis* in one of the cases reported, and we might add almost all possible intercurrent diseases, especially *pulmonary tuberculosis* and acute *pneumonia*, which have been repeatedly observed. Wunderlich saw two cases complicated with *diphtheritic affection of the throat*.

Diagnosis.

In the commencing stage a sure diagnosis is not possible, even if the disease begins in external lymphatic glands accessible to the observer.

The essential criterion of malignity must be sought for in the rapid growth of the tumors and the progressive invasion of new clusters of glands by the disease, which can be made out only by continued watching of its course. From *scrofulous* glandular swellings it is distinguished by the absence of periadenitis, cheesy degeneration, and softening, so frequent in those; even the hard variety of malignant lymphoma is characterized by a certain elasticity, which cannot be compared with the board-like hardness of the cheesy gland, before softening has commenced in it.

Lymphatic glands, secondarily affected with *carcinoma*, show much more resemblance to malignant lymphoma, and mistakes may occur for a time, if the primary seat of carcinoma cannot be made out; but in their later course the two diseases diverge considerably.

The diagnosis between soft lymphoma and the lymphatic form of leukhæmia can be made with certainty only by means of a microscopical examination of the blood.

Finally, the *sarcoma* proper of the lymphatic glands must be mentioned. The diagnosis between this and malignant lymphoma is attended with difficulty, on account of the confusion in the nomenclature above alluded to, and also on account of the transitions from one into the other. From the reasons already mentioned, we deem it necessary to separate malignant lymphoma from sarcoma of the lymphatic glands, and would base the essential difference, with Winiwarter, on the general fact that lymphoma consists in a hyperplastic process, while only such tumors are to be regarded as sarcomatous, the type of which has nothing in common with the mother-tissue. It is true, however, that this difference is not actually always well marked, as the soft lymphoma is very nearly allied to some varieties of spheroidal-cell sarcoma, while the hard approaches in its histological characters some forms of fibro-sarcoma.

Everybody who has occasion to gather experience in these matters must, however, be impressed with the conviction that in the majority of cases there are enough criteria present which enable us to distinguish malignant lymphoma from sarcomatous glands. On this difference in the behavior of sarcoma proper of the lymphatic glands, R. Schulz has even based the proposition to substitute the designation "*desmoid carcinoma*" for lymphoma and lymphosarcoma. He points out correctly that the species of tumor with which we are occupied bears, in spite of its apparently local origin, rather the character of a *general disease of the lymphatic tissues*, while in sarcoma proper the disease is at first *strictly local*, and, as a rule, invades by metastasis not the lymphatic apparatus, but pretty uniformly the whole body. The extension takes place in the latter case probably by means of the blood-current.

These differences are practically important, inasmuch as extirpation of the local tumor holds out no hope of success in *malignant lymphoma*, because the disease has already invaded too many groups of glands, while a timely removal of a *sarcomatous* gland may be probably successful whenever complete local extirpation can be accomplished.

We have to consider, furthermore, that sarcoma extends more frequently to the neighboring tissues in a direct manner, and is, to a much greater degree than malignant lymphoma, disposed to retrograde metamorphoses and to ulceration. We shall not describe in detail the differences in a histological point of view ; it must be sufficient to mention that almost every type of sarcoma (the large-celled and small-celled, round-celled and fusiform-celled, the endothelial, myxomatous, melanotic, etc.) may occur in the lymphatic glands. It is well, therefore, not to designate any sarcoma of the lymphatic glands, even the primary one, as lymphosarcoma, and much more correct to speak only of *sarcoma of the lymphatic glands*, and to add, if possible, the accurate designation of the special form.

Duration, Termination, Prognosis.

The course of malignant lymphoma is comparatively rapid, especially so if compared with leukhæmia.

In some cases it lasts only from two to six months, in the majority about one year ; cases of over three years' duration are very rare.

Termination in recovery has not been reported, we might say, in any case up to the most recent time, for Wunderlich's case which terminated favorably cannot with certainty be called one of malignant lymphoma. Within the last few years, however, new therapeutical efforts seem to have been more successful. As long as our experience does not extend to a greater number of favorable cases we are obliged to call the *prognosis* of this disease as exceedingly unfavorable, and in this regard its designation as cancer cannot be objected to.[1]

Treatment.

The *surgical* treatment of malignant lymphoma must be pronounced as hopeless, on the ground of the experience gained thus far. The patients are generally very little troubled by the first symptoms of their disease, and even the professional attendant mostly believes the tumors to be of a simple hyperplastic character, and consequently prescribes merely an iodine ointment or some such local remedy. At this stage it would also be hardly possible to persuade the patient to submit to an operation. Very soon, however, the disease has so far extended that every idea of an operative interference is discarded.

Electrolysis has been vaunted as a successful remedy by some writers, but more reliable experience has proved that no better results are attained by it than by extirpation.

It is easily understood, therefore, why the greater number of reported cases have been treated medicinally.

Among the internal remedies *quinine*, *mercury*, and *iodide of potassium* have been repeatedly tried, but all without success, if we except the above-mentioned case of Wunderlich, which improved on the use of iodide of potassium. We can add as the result of our own experience that the internal use of *carbolic acid* produced no effect whatsoever.

A series of cases has been reported on the other hand as cured, or at least improved by treatment with *arsenic.* This mode of treatment being new, a more detailed description of it may seem justifiable.

The first experience of this kind has been published by Billroth,[2] whose patient, a woman aged forty, had been sick already for ten months with enlargement of the cervical, axillary, and inguinal glands, to the size of from a hen's egg to a fist. Quinine (up to scruple doses) remained without effect. After administration of *Fowler's solution* the glands began to diminish in size already within a fortnight, and when the patient was dismissed two months afterwards there remained only one gland on each side of the neck enlarged to the size of a filbert.

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[1] *R. Schulz* suggests accordingly that Leukhæmia might also be considered as a "chronic desmoid carcinoma."

[2] Wiener Med. Wochenschrift. 1871. No. 14.

According to Winiwarter's communication Fowler's solution was given in five other analogous cases of Billroth's clinic; in three of them there was no appreciable result; in one the glands diminished rapidly, but the patient died in consequence of phlegmonous erysipelas following the extirpation of a small gland in the neck for diagnostic purposes, and one case remained still under treatment at the time of publication of the communication.

Of four cases of Czerny's clinic, reported by Tholen (l. c.), a cure was effected in two; in one the tumors were reduced rapidly, but the patient died of marasmus; and in the fourth the treatment remained without effect.

In reference to the mode of administering the arsenic, we reproduce the following statements of Winiwarter:

The patient had to take in the beginning of the treatment five drops a day of a mixture consisting of equal parts of Fowler's solution and the compound tincture of gentian. In periods of two or three days the dose was increased to 10, 15, 24, and 40 drops, and then again diminished in similar proportion. If signs of toxical effects appeared the treatment was interrupted for a time.

The treatment lasted in one case, which was cured, fifty-three days, in others longer. The total quantity of arsenious acid consumed amounted in the cured case to 19.8 grammes (305 grains).

The patients bore the remedy without trouble during the first days. The first symptom of its effect on the glands was softening and greater mobility, and after about eight or ten days the tumors became painful almost without exception. Later on rapid diminution of the glands was observed in the case in which the treatment was successful, they became at the same time harder and firmer, and their sensitiveness died away gradually. In one case inflammation and suppuration of the tumors ensued.

Among other symptoms we have to mention especially the fever which appeared regularly under this treatment (even when the tumors diminished in size). Already after the fourth or fifth dose the temperature rose (101.3°-103.1° F.) every evening, descending to the normal standard in the morning. When the treatment was interrupted the fever would still last a couple of days. Suffusion of the cheeks, increasing appetite at first, increased thirst, later on abdominal pain, sometimes vomiting, diarrhœa, burning sensations in the rectum, great emaciation also appear during the treatment.

Czerny employed in a case which terminated favorably parenchymatous injection of Fowler's solution, besides its internal administration. This was also tried in a case of Billroth's clinic reported by Winiwarter (from 1 to 9 drops of the solution were injected into the tumors), but the success was incomplete; when afterwards the remedy was given internally (increasing from 1 to 30 drops) complete reduction of the tumors was effected.

Although we cannot as yet regard arsenic as a certain remedy against malignant lymphoma we have still to welcome with vivid satisfaction this addition to our therapeutical remedies against a disease almost absolutely fatal heretofore. Let us hope that the successful cases reported thus far may be increased by numerous additions, and that the curative effects of this remedy may prove themselves as permanent—a hope not yet certain of fulfilment if we may judge from what we know about them at the present time.

DIABETES MELLITUS AND INSIPIDUS.

SENATOR.

LEEDS & WEST-RIDING
CHIRURGICAL SOCIETY

DIABETES MELLITUS.

THE literature of Diabetes is too extensive to admit of a complete summary here. For the earlier literature, of which I mention only the most important works, reference may be had to the historical accounts by *Hirsch*, Handb. der historisch-geographischen Pathologie. Erlangen, 1860. S. 568.—*Haeser*, Lehrb. der Geschichte der Medicin. 3. Aufl. I. 1874.—*M. Salomon*, Geschichte der Glycosurie u. s. w. Deutsches Arch. f. klin. Med. VIII. S. 489.—Also *Copland*, Dict. of Pract. Med., Vol. I., 507, and *Canstatt*, Handb. d. med. Klinik. III. 1846. 804.

Thomas Willis, Pharmaceut. ration. Oxford, 1674, and Amstelodami, 1682. Sect. IV. Cap. III.—*Matthæus Dobson*, Medic. Observations by a Society of Physic. in London, 1775. V. p. 298. Germ. Altenburg, 1778.—*Francis Home*, Klinische Versuche u. s. w. Aus dem Englischen. Leipzig, 1781.—*Th. Cowley*, London Med. Journ. IX. 1788.—*J. Rollo*, On Diabetes Mellitus. London, 1797, and Abhandl. über Diab. mell. mit chem. Versuchen von *W. Cruikshank*. Wien, 1801, and Stendal, 1801.—*J. P. Frank*, De curandis hom. morbis epitome. Lib. V. De profluviis. Pars. I. Manhemii, 1794. p. 38–67.—*Marabelli*, Mem. sull. differenze dell'orina in diab. Pav. 1792.—*Pelham Warren*, Med. Transact. of the College of Physicians, 1812. IV. p. 188.—*Vauquelin* et *Ségalas*, Magendie's Journal de Physiol. 1825. IV. p. 356 and 825.—*W. Prout*, (a) Inquiry into the nature and treatment of diab., calculus, etc. 2. ed. London, 1825. (b) On the nature and treatment of stomach and renal diseases. London, 1848, and subsequent editions.—*Venables*, A pract. treat. on diab. London, 1825.—*F. A. G. Berndt*, Encycl. Wörterb. IX. S. 310.—*Lehmann*, Diss. de urina diab. Leipzig, 1835.—*Maitland*, London Med. Gaz. XVII. 1836. 5. March.—*O. Rees*, Guy's Hosp. Rep. 1838. III. p. 398.—*M'Gregor*, London Med. Gaz. 1837. May.—*Corneliani*, Opusculo sul diab. Pavia, 1840, and in Giornale per servire ai progr. dell pat. e della terap. 1841. p. 328.—*Christison*, Edinb. Monthly Journ. 1841. April, etc.—*Bouchardat*, Gaz. méd. 1835. No. 11. Revue méd. 1839. Juin. Annuaire de Thérap. 1842, 1846, 1848. Clinique européenne, 1859, No. 58.—Des troubles de l'innervation chez les glycosuriques. Bull. de Thér. 1875. LXXXVIII. p. 145.—Considér. gén. sur le traitement hyg. de la glycosurie. *Ibid.*, LXXXIX. S. 97.—*C. Liman*, Obs. quaedam de d. mell. Diss. Halae, 1842.—*Genzke*, Hygicia. XVIII. II. 2.—*Vogt*, Einige Beobacht. und Bemerk. über die honigartige Harnruhr. Henle's u. Pfeuffer's Zeitschr. f. rat. Med. 1844. I. S. 147.—*Cappezuoli*, Gaz. méd. 1845.—*Mialhe*, Compt. rend. 1844, 1845, 1851. p. 33, etc. Gaz. méd. 1846, No. 16. Bull. de Thérap. 1849, Mars. Gaz. méd. de Paris, 1866. p. 319.—*G. W. Scharlau*, Die Zuckerharnruhr. Berlin, 1846.—*Fletcher*, Med. Times, 1847. July. p. 394.—*J. Henle*, Handb. der rat. Path. II. 1847. S. 344.—*Brand*, Mittheilungen aus der med. Klinik des Prof. *Canstatt.* Deutsche Klinik. 1850. No. 6.—H. *Nasse*, Archiv f. physiol. Heilk. 1851. X. 1, and Untersuch. zur Physiol. u. Pathol. I. S. 300.—*Miquel*, Ueber D. m. Archiv f. physiol. Heilk. X. 1851. S. 479.—*M. Traube*, (a) Ueber die Verdauung des Fettes im D. m. in Virchow's und Reinhardt's Archiv IV. 1851. S. 148. (b) Ueber die Gesetze der Zuckerausscheidung im D. m. *Ibid.*, S. 109.—*Drummond*, Monthly Journal of Med. 1852. XIV. p. 281.—*Frick*, A case of D. m. with remarks, etc. Amer. Journ. of Med. Sc. 1852. XXIV. p. 64.—*C. Ph. Falck*, Zur Kenntniss der Zuckerharnruhr. Deutsche Klinik. 1853. No. 22 et seq.—*L. Beale*, On the chemical and microscopical conditions of the liver and kidneys, etc. Brit. Review. 1853. July.—*F. W. Boecker*, Deutsche Klinik. 1853. No. 33-35.—*Marchal de Calvi*, Comptes rendus. XXXVII. p. 25, and XLIII. p. 1006; also, Recherches sur les accidents diabétiques. Paris, 1864.—*R. Leupoldt*, Ueber die Harnruhr. Diss. Erlangen, 1853.—*v. Dusch*, Ztschr. f. rat. Med. 1853. IV. 1.—*Bence Jones*, Med. Chir. Transact. XXXVI. Dublin Hosp. Gaz. 1858. 174.—Med. Times and Gaz. 1865.—*Marsh*, Dublin Journ. of Med. Sc. 1854. XVII. p. 1.—*F. Th. Schulze*, in Virch. Arch. VII. S. 397.—*Andral*, (a) Comptes rend. 1855. Juilliet. (b) Documents pour servir à l'hist. de la glycosurie. La France méd. 1875. No. 30.—*Heller*, Wiener med. Zeitschr. 1850. VI. 1; in his Archiv, 1852, see Schmidt's Jahrb. LXXXI. S. 193.—*P. Montegazza*, Zur Physiol. und Pathol. des D. m. Gaz. Lomb. 1854. 1. s. Schmidt's Jahrb. LXXXV. S. 302.—*Semmola*, Comptes rend. 1855. 10. Sept.—*S. Rosenstein*, Virchow's Archiv. XII. S. 414 u. 430.—*A. Wagner*, Beitrag zur Kenntniss der Beziehungen zwischen der Mellit. und Carbunkel. *Ibid.*, S. 401 u. 462.—*Hodgkin*, see Schmidt's Jahrb. LXXXVI. S. 187.—*W. Petters*, Beob. an 5 Diabeteskranken, Prager Vierteljahrschr. 1855. XLII. 2 u. 1857. LV. 81.—*Stockvis*, Bijdragen to de kennis der zuckervorming in de lever 1856, and Wiener med. Wochenschr. 1857. No. 14.—*A. Guenzler*, Ueber D. m. Dissert. Tübingen, 1856.—*A. Ott*, Beitr. zur Therapie der Zuckerharnruhr. Dissert. Tübingen, 1857.—*Jordaô*, Considér. sur un cas de diabète. Thèse. Paris. 1857.—*Fauconneau-Dufresne*, Gaz. hebd. 1857. Juin, etc., and Union méd. 1868. No. 37.—*E. Wiederhold*, Deutsche Klinik. 1857. No. 41.—*Leconte*, Archives gén. 1857. Août.—*Harley*, *ibid.*, 1857. Septbr.—*Thierfelder* u. *Uhle*, Ueber die Harnstoffausscheidung im D. m. Archiv der Heilk. 1858. S. 32.—*Gibb*, Med. Times and Gaz. 1858. July. p. 21.—*Griesinger*, Studien über Diabetes. Archiv für physiol. Heilk. 1859. N. F. III. S. 1.—*Folwarczny*, Leberanalysen bei D. m. Wiener Zeitschr. N. F. 1859. II. 6.—*v. Maack*, Zur Therapie des D. m. Archiv des Vereins f. gemeinsch. Arbeiten, 1860. V. S. 129.—*Kaulich*, Prager Vierteljahrschrift. 1860. LXVII. 58.—*F. W. Pavy*, (a) Philosoph. Transactions, 1860; (b)

Researches on the Nature and Treatment of Diabetes. London, 1862; (c) Cases illustrating the influence of opium and some of its constituent principles, etc. Guy's Hosp. Reports, 1870. XV. p. 420; (d) The Lancet, 1874. 29. Aug. and Brit. Med. Journ. 1875. No. 758.—*J. Vogel* in Virchow's Hand. der spec. Path. Bd. VI. 2. S. 478.—*Weikart*, Arch. d. Heilk. 1861. S. 173.—*Hartsen*, Donders, Archiv f. d. holländ. Beitr. III. S. 319.—*E. Neuschler*, Beitrag zur Kenntniss der einf. und der zuckerführenden Harnruhr. Diss. Tübingen, 1861.—*Haughton*, On the phenomena of the D. m. Dublin Journal of M. Sc. 1861. Octob., Novbr.—*F. Betz*, (a) Ueber Acetonämie. Memorabilien für pract. Aerzte, 1861. VI. 3; (b) Erster Bericht über D. m. in Württemberg. Württ. med. Corresp.-Bl. 1872. Nr. 4.—*Clark*, Amer. Med. Times, N. S. 1862. IV. No. 23. etc.—*Winogradoff*, Beitr. zur Lehre vom D. m. Virchow's Archiv XXVII. S. 533.—*Stopczanski*, Ueber Bestimmung des Kreatinins im Harn und Verwerthung desselben beim D. m. Wiener med. Wochenschr. 1863. Nr. 21–25.—*Grohe*, Der Chylus ein Ferment. Greifsw. med. Beitr. 1864. III. S. 1.—*Bartels*, Ber. über die 39. Naturforscher-Versamml. Giessen, 1864.—*Cantani*, (a) Ueber Acetonämie. Il Morgagni, 1864. VI. p. 365; (b) Casi guariti di diabeti mellito. *idem*, 1872.—*F. Mosler*, (a) Ueber Beschaffenheit des Parotidensecrets bei D. m. Archiv der Heilk. 1864. S. 228; (b) Unters. über Beschaffenheit des Parotidensecrets u. s. w. Berliner klin. Wochenschr. 1866. Nr. 16 et seq.; (c) Kleinhirnläsion bei D. m. Deutsch. Archiv f. klin. Med. XV. S. 229.—*M. Pettenkofer* and *C. Voit*, (a) Ueber das Wesen der Zuckerharnruhr. Sitzgsb. d. Münchener Acad. 1865. Nov. S. 224; (b) Ueber den Stoffverbrauch bei der Zuckerharnruhr. Zeitschr. f. Biol. 1867. III. S. 380 et seq.—*Smoler*, Prager Vierteljahrschr. LXXXII. S. 46 et seq.—*F. v. Recklinghausen*, Drei Fälle von D. m. Virchow's Archiv XXX. S. 360.—*Friedreich*, Ueber das constante Vorkommen von Pilzen bei D. m. *Ibid.*, S. 476.—*W. Kuehne*, Ueber das Vorkommen zuckerbildender Substanzen, etc. *Ibid.*, XXXII. S. 536.—*J. Seegen*, (a) Beitr. zur Casuistik des D. m. *Ibid.*, XXXVI. S. 227; (b) Oestr. Zeitschr. f. Heilk. 1865. Nr. 11; (c) Wiener med. Wochenschr. 1866. Nr. 23 et seq.; (d) der D. m. auf Grundlage zahlreicher Beobachtungen (Monographie). Berlin, 1870. II. Aufl. 1875.—*L. Fleckles*, (a) Ueber D. m. mit besonderer Berücksichtigung balneo-therapeutischer Erfahrungen. Prag, 1865. (b) Zur Pathogenese und Balneotherapie des D. m. Leipzig, 1871.—*A. Ruickoldt*, Ein Beitrag zur Lehre von der Zuckerharnruhr. Diss. Jena, 1865.—*Burresi*, Journal de méd. de Bruxelles, 1865. p. 522.—*Wallach*, D. m. von 5 wöchentlichem Verlauf. Virchow's Archiv XXXVI. S. 297.—*C. Gaethgens*, (a) Ueber den Stoffwechsel eines Diabetikers, verglichen mit dem eines Gesunden. Diss. Dorpat, 1866; (b) Ueber Kreatinin- und Harnsäure-Ausscheidung in einem fieberhaft und tödtlich verlaufenen Fall von D. m. Hoppe-Seyler's med. chem. Untersuch. Berlin, 1868. 3 Heft. S. 301.—*Verneuil*, De la gangrène diabétique et du traumatisme chez les diab. Union méd. 1866. Nos. 142 et seq.—*F. C. Helfreich*, Zur Pathogenese des D. m. Diss. Würzburg, 1866.—*M. Jaffé*, Ueber das Vorkommen zuckerbildender Substanzen in den Organen der Diabetiker.

Virchow's Archiv XXXVI. S. 20.—*K. Zimmer*, (a) Ein Beitrag z. Lehre vom D. Deutsche Klinik. 1867. Nr. 14; (b) Die nächste Ursache des D. m. *Ibid.* 1871. Nr. 5; (c) Der. D. m., sein Wesen und seine Behandlung. 1 Heft. Leipzig, 1781; (d) Die Muskeln, eine Quelle des Z. im D. m. Deutsche Klinik. 1873. Nr. 7.—*R. Beckler*, Rascher Verlauf von D. m. Bayer. ärztl. Int.-Bl. 1868. Nr. 11.—*H. Huppert*, Ueber die Glycosurie bei Cholera mit Bemerkungen über die Zuckerh. Archiv d. Heilk. 1867. VIII. S. 331.—*v. Duering*, Ursache und Heilung des D. m. Hannover, 1868. II. Aufl. 1875.—*M. Popper*. Das Verhältniss des D. zu Pankreasleiden und Fettsucht. Oestr. Zeitschr. für praktische Heilk. 1868. Nr. 11.—*Naunyn* und *Riess*, Ueber Harnsäureausscheidung. Reichert's und du Bois-Reymond's Archiv. 1869. S. 381.—*Muench*, D. mell.—chronisches Leberleiden. Moskauer med. Ztg. 1869. Nr. 37.—*Durand-Fardel*, (a) Note sur la pathol. du D. Bull. de l'ac. de méd. 1869. XXXIV. p. 229; (b) Traité clinique et thérap. du D. Paris, 1869.—*J. B. Dompeling*, D. m. en paresis des rechter ledematen tengefolge van en tumor med. obl. Nederl. Arch. voor Geenesk. 1869. IV. p. 179.—*B. Foster*, (a) Note on temperature in D. Journ. of Anat. and Physiol. 1869, May; (b) Observations on D. m. and its treatment. Brit. and Foreign Med. Chir. Review. 1872, Octbr.; and in Clinical Lectures. London, 1874. p. 194 et seq.—*W. Leube*, Zur Path. und Ther. des D. Deutsches Archiv für klin. Med. V. S. 372. —*A. S. Donkin*, (a) On a Purely Milk Diet in the Treatment of D. M., etc. The Lancet, 1869. II. No. 22; 1871. I. p. 603; 1873. I. No. 2 and 3; (b) On the Relation between D. and Food, etc. London, 1875.—*Ossowidski*, Ueber die bei der Zuckerharnr. vorkommenden Augenkrankheiten. Diss. Berlin, 1870. —*Dutcher*, A Lecture on D. M. Philad. Med. and Surg. Reporter. 1870. XXII. No. 1-3.—*H. Dickinson*, (a) On Certain Morbid Changes in the Nervous System associated with D. M. Med. Times and Gaz. 1870. March 9, and Brit. Med. Journ. 1870. Feb. 16; (b) Diseases of the Kidney. I. Diab. London, 1875.—*R. Hein*, Zur Lehre vom D. M. (Description of a Complicated Case, etc.). Deutsches Arch. f. klin. Med. S. 42.—*W. F. Smith*, Case of Acute D., with Remarks. Brit. Med. Journ. 1871. Decbr. 23.—*W. Richardson*, Remarks on D., especially with reference to Treatment. London, 1871.—*W. Wadham*, On the Relative Influence of Bread, Honey, and Sugar upon the Amount of Urea and Sugar excreted in D. St. George's Hosp. Rep. 1871. V. 193.—*Devergie* et *Foville Fils*, Du traitement du D. au moyen de l'arsenic. Gaz. med. 1870. No. 22, and Paris, 1871.—*G. M. Smith*, On D. New York Med. Record. 1871. March 15.—*Kratschmer*, (a) Ueber die Wirkung des Opiums und Morphiums bei D. m. Wiener med. Wochenschr. 1871. Nr. 8; (b) Ueber Zucker- und Harnstoffausscheidung beim D. m. unter dem Einfluss von Morphium, kohlens. und schwefels. Natron. Ibid. 1873. Nr. 20.—*O. Schultzen*, Beitr. zur Pathol. und Therapie des D. m. Berliner klin. Wochenschr. 1872. Nr. 35.—*E. Kuelz*, (a) Ueber Harnsäureausscheidung in einem Fall von D. m. Diss. Marburg, 1872; (b) Beiträge zur Hydrurie und Melliturie. Habilitationsschrift. Marburg, 1872; (c) Studien über D. m. und insip. Deutsches Archiv für

klin. Med. XII. S. 248; (d) Beiträge zur Path. u. Ther. des D. m. I. Bd. Marburg, 1874; II. Marburg, 1875.—*A. de Fleury*, Théorie du D. Gaz. hebd. de méd. et de chir. 1872. Nr. 33.—*Fischer*, D. m. in Folge einer Lebererschütterung mit tödlichem Ausgange. Zeitschr. f. Wundärzte und Geburtsh. 1872. 1.—*G. Primavera*, Il d. m. de il Prof. *Cantani*, Il Morgagni, 1872. Diss. X.—*V. Budde*, Om d. m. med. särligt Hensyntil dens Behandling. Afhandling for Doktorgraden. Kopenhagen, 1872.—*Popoff*, Vergleichende Untersuchungen über die Wirkungen einiger Arzneistoffe bei der Zuckerh. Berl. klin. Wochenschr. 1872. Nr. 28. 17.—*M. Duboue*, De l'odeur acide de l'haleine comme signe diagnostique du D. Gaz. des hôpit. 1872. No. 101.—*Senator*, Ueber D. m. bei Kindern. Berl. klin. Wochenschr. 1872. No. 48. Sitzungsbericht der Berl. med. Ges.—*Th. Niedergesaess*, D. m. infantum. Diss. Berlin, 1873.—*E. Bertail*, Étude sur la phthisie diabétique. Paris, 1873. *F. Kretschy*, Ueber D. m. Wiener med. Wochenschr. 1873. Nr. 3.—*O. M. Lecorché*, Considér. théorétiques et thérap. sur le d. s. Gaz. hebdom. de méd. et de chir. 1873. Nr. 24–27.—*E. Bischoff*, Ein Beitrag zur Path. und Ther. des D. m. Bayer. ärztl. Int.-Bl. 1873. Nr. 23.—*R. Schmitz*, (a) Vier Fälle von geheiltem D. m. und kurze Bemerkungen über die Entstehung desselben. Berliner klin. Wochenschr. 1873. Nrs. 18 and 19; (b) Zur Aetiol. des D. m. *Ibid.*, 1874. Nr. 44.—*A. Boettcher*, Sectionsbefund bei einem an D. m. gestorbenen Manne. Dorpater med. Zeitschr. 1873. IV. S. 172.—*J. Blumenthal*, Zur Therapie des D. m. Berliner klin. Wochenschr. 1873. Nr. 13.—*F. Buerger*, Ueber die Perspiratio insensibilis bei D. m. und insip. Deutsches Archiv für klin. Med. XI. S. 323.—*W. L. Lehmann*, Het Arzenigzuur als Geneesmittel by D. m. Academ proefschrift. Amsterdam, 1873.—*W. Ebstein* und *Jul. Mueller*, Ueber die Beh. der Zuckerh. mit Carbolsäure. Berliner klin. Wochenschr. 1873. Nr. 43, and Verhdl. der Ges. der Naturforscher und Aerzte. 1874. zu Breslau. S. 103. Weitere Mittheilungen über die Beh. etc. nebst Bemerkungen über d. Anwendung der Salicylsäure. Berl. klin. Wochenschr. 1875. Nr. 5.—*Kaemnitz*, Ueber einen Fall von Kopfverletzung mit folgendem D. m. Arch. d. Heilk. XIV. 5 Heft.—*Harnack*, Zur Pathogenese des D. m. Diss. Dorpat, 1873, and Deutsches Arch. für klin. Med. XIII. S. 593.—*Lauder Brunton*, Lectures on the Path. and Treatment of D. M. Brit. Med. Jour. 1874. Nrs. 1, 39, and 121.—*Tomasi*, Contribuzione alla casuistica del D. m. Il Morgagni. 1874. Disp. II.—*G. Schleich*, Erfahrungen über diätet. Behandlung bei D. m. Würtemb. med. Corr.-Bl. 1874. Nr. 34.—*Kraussold*, Zur Path. und Ther. des D. m. Diss. Erlangen, 1874.—*Kussmaul*, Zur Lehre vom D. m. Ueber eine eigenthümliche Todesart bei Diabetischen, über Acetonämie; Glycerinbehandl. und Einspritzungen von Diastase ins Blut bei dieser Krankheit. Deutsches Archiv für klin. Med. XIV. S. 1.—*F. Rupstein*, Ueber das Auftreten des Acetons beim D. m. Centralbl. für die med. Wiss. 1874. S. 865.—*F. W. Beneke*, Grundlinien der Path. des Stoffwechsels. Berlin, 1874. S. 296.—*Bourneville* et *Teinturier*, Du coma diabétique. Le progrès méd. 1875. No. 8.—*L. Blau*, Ueber D. m. und insip. (Abstract) Schmidt's Jahrb. CLXV. S.

185, and CLXVI. S. 178.—*J. Mayer*, Beitr. z. Symptomat u. Ther. des D. m. Berl. klin. Wochenschr. 1875. Nrs. 22 and 23.—*Boese*, Zur D.-Behandlung. Deutsch. Arch. f. klin. Med. XVI. S. 96.—*Adrian van Traa*, Over de behandeling von D. m. Diss. Leiden, 1875.

PHYSIOLOGICAL: *Frerichs*, (a) Beitr. z. phys. u. path. Chemie d. Galle, 1845. (b) Verdauung in Wagner's Handwörterb. der Physiol. III. S. 831.—*Cl. Bernard* and *Barreswil*, Arch. gén. de. méd. 1848. Octobr. Comptes rendus. 1848. XXVII. p. 514; and XXXI. p. 572.—*Cl. Bernard*, Mémoires de la soc. de biol. 1849. I. p. 221.—Nouvelles fonctions du foie considérée comme l'organe producteur de matière sucrée. Paris, 1853. German by Schwarzenbach, 1853. Leçons de physiol. expérimentale appliquée à la médecine. Paris, 1854–1855. I. Leçons sur les propriétés des fluides. 1859. II. Leçons sur la physiol. et path. du système nerveux. Paris, 1858. I. p. 401 et seq. Comptes rendus. 1859. LXVIII. p. 884 et seq. Revue scientifique de la France et de l'étranger. 1873. p. 1111; 1874. p. 519, etc.—*C. G. Lehmann*, Ber. der k. s. Ges. zu Leipzig, 1850. III. S. 139; 1856. VII. S. 2. Zoochemie. Leipzig, 1858, etc.—*A. Sanson*, Compt. rend. XLIV. 1159 et seq.; and Journ. de Phys. I. p. 244.—*Colin*, Compt. rend. XLIX.—*J. P. Uhle*, De saccharo in urinam aliquamdiu transeunte. Diss. Leipzig, 1852.—*L. Schrader*, Die Erzeugung des D. bei Kaninchen durch Verletzung einer Stelle, etc. Göttinger gel. Nachrichten, 1852. März.—*F. J. v. Becker*, Ueber das Verhalten des Zuckers beim thierischen Stoffwechsel. Zeitschr. f. wiss. Zoologie, 1853. V. 2.—*Poggiale*, Comptes rendus. XLII. p. 198; and Gaz. méd. de Paris. 1856. Nr. 6.—*W. Kuehne*, Ueber künstl. D. bei Fröschen. Diss. Göttingen, 1856; Lehrb. der phys. Chemie. Leipzig, 1868. S. 62 et seq. and 516 et seq.—*V. Hensen*, Verhdlg. der Würzb. phys. med. Ges. 1856. VII. S. 219; and Virchow's Archiv. XI. S. 395.—*Schiff*, (a) Nachrichten der Ges. der Wiss. zu Göttingen, 1856. S. 241; (b) Unters. über die Zuckerbildung in der Leber. Würzburg, 1859. Arch. f. phys. Heilk. N. F. I. S. 263; (c) Comptes. rend. XLVIII. p. 880; (d) Sulla glycogenia animale. Firenze, 1866; (e) Nouvelles recherches sur la glycogénie anim. in Journ. de l'anat. et de phys. 1866. p. 354.—*F. W. Pavy*, Guy's Hosp. Rep. 1855. III. p. 1. On the Assimilation of Sugar by the Liver. Med. Times and Gaz. 1865. I. p. 353 et seq.—*Heynsius*, Studien des physiol. Instituts zu Amsterdam, 1861.—*Ritter*, Ueber die Amylum und den Zucker der Leber. Zeitschr. f. rat. Med. 3. Reihe. XXIV. S. 65.—*R. Mac Donnel*, On the Amyloid Substance of the Liver. Amer. Journ. of Med. Sc. 1863. XLVI. p. 523; Comptes rendus. LX. 963, etc.; Observations on the Function of the Liver. Dublin, 1865.—*E. Eckhard*, (a) Die Stellung der Nerven beim künstlichen D. Beiträge zur Anat. und Physiol. 1867. IV. S. 1; (b) Untersuchungen über Hydrurie. *Ibid.* 1870 and 1871. VI. S. 1 and S. 53.—*M. Tscherinoff*, Ueber die Abhängigkeit des Glykogengehalts der Leber von der Ernährung. Wiener ak. Sitzgsber. 1865. LI. 2. S. 412; Centralbl. f. d. med. Wiss. 1865. Nr. 5; Virchow's Archiv XLVII. S. 102.—*Saikowsky*, Zur Diabetesfrage. Centralbl.

f. d. med. Wissensch. 1865. S. 769; 1867. S. 65.—*O. Nasse*, De materiis amylaceis num in sanguine inveniantur. Habil.-Schrift. Halle, 1866.—*A. Eulenburg*, Zur Frage über die Zuckerbildung in der Leber. Vierteljhrschr. der naturf. Ges. in Zürich, 1867. XII. S. 232, and Berlin klin. Wochenschr. 1867. Nr. 41.—*A. E. W. Tieffenbach*, Ueber die Existenz der glykogenen Function der Leber. Diss. Königsberg, 1869.—*L. Senff*, Ueber den D. nach Kohlenoxydathmung. Diss. Dorpat, 1869.—*Schtscherbakoff*, Ueber Glykogen. Bericht der deutschen chem. Ges. 1870. S. 200.—*W. T. Lusk*, On the Origin of D. New York Med. Journ. 1870. July.—*J. C. Dalton*, Sugar Formation in the Liver. Transact. of the New York Academy, 1871.—*C. Bock* and *F. A. Hoffmann*, (a) Ueber eine neue Entstehungsweise von Melliturie. Archiv von Reichert und du Bois-Reymond. 1871. S. 550; (b) Ueber das mikrochem. Verhalten der Leberzellen. Virchow's Archiv. 1872. LVI. S. 201; (c) Experimental-Studien über D. Berlin, 1874.—*E. Bruecke*, Ueber eine neue Methode, Dextrin und Glykogen etc. abzuscheiden, und über einige damit erlangte Resultate. Wiener acad. Sitzungsber. 1871, Febr.—*Weiss*, Zur Statik des Glykogens im Thierkörper. *Ibid.* Juli.—*B. Luchsinger*, (a) Zur Glykogenbildung in der Leber. Centralbl. für die med. Wiss. 1872. S. 131, and Pflüger's Arch. VIII. S. 289; (b) Experimentelle und kritische Beitr. z. Physiol. und Pathol. des Glykogens. Diss. Zürich, 1875.—*F. W. Dock*, Uber die Glykogenbildung in der Leber und ihre Beziehung zum D. Pflüger's Archiv V. S. 571.—v. *Wittich*, (a) Ueber das Leberferment. *Ibid.* VII. S. 28; (b) Zur Statik des Leberglykogens. Centralbl. f. d. med. Wiss. 1875. S. 113; (c) Ueber den Glykogengehalt der Leber nach Unterbindung des Ductus choledoch. *Ibid.* S. 291.—*E. Tiegel*, Ueber eine Fermententwicklung des Blutes. *Ibid.* VI. S. 249.—*E. Cyon* and *Aladoff*, Die Rolle der Nerven bei Erzeugung von künstl. D. m. Bull. de l'acad. de Petersbourg. VIII. p. 91.—*P. Kuentzel*, Exp. Beiträge zur Lehre von der Mellit. Diss. Berlin, 1872.—*H. Jeanneret*, L'urée dans le d. artificiel. Diss. Bern, 1872.—*Moriggia*, Alcune sperienze intorno al glucosio etc. Reale Acad. dei Lincei. III. 1873. 9. Febr.—*L. Seelig*, Vergleichende Untersuchungen über den Zuckerverbrauch im diabetischen und nicht diabetischen Thiere. Diss. Königsberg, 1873.—*E. Schoepffer*, Beiträge zur Kenntniss der Glykogenbildung in der Leber. Archiv f. exp. Path. 1873. I. S. 72.—*S. Weiss*. Ueber die Quelle des Leberglykogens. Wiener acad. Sitzungsber. LXVII. 3. Abth.—*G. Salomon*, (a) Ueber die Bildung des Glykogens in der Leber. Centralbl. f. d. med. Wiss. 1874. S. 179, and Virchow's Archiv. LXI. S. 343; (b) der Glykogengehalt beim neugeboren Kinde. *Ibid.* S. 739.—*L. Goldstein*, Beiträge zur Lehre von der Glykogenbildung in der Leber. Würzburger phys.-med. Verhandl. 1874. VII. S. 1.—*H. Pink*, Zur Lehre vom D. m., insonderheit zur Lehre von der Glykogenbildung. Diss. Königsberg, 1874.—*G. Heidenhain*, Ein Beitrag zur Lehre des D. m., insonderheit etc. Diss. Königsberg, 1874.—*Wickham Legg*, Ueber die Folgen des D.-Stiches nach dem Zuschnüren der Gallengänge. Archiv für exp. Pathol. 1874. II. S. 384.—*Naunyn*, Beiträge zur Lehre vom D. m. Archiv für exp. Path. III. S. 83.—*Durand-Fardel*, Étude

critique de la physiologie pathologique du diabète. Gaz. méd. de Paris. 1875. No. 20 et seq.

Historical Introduction.

The name of *diabetes mellitus* (mellituria, glycosuria, Zuckerharnruhr) is applied to a disease which is generally chronic in its course, and which is characterized by a long-continued excretion of grape-sugar in the urine, and usually by an increase in the quantity of the urine. By its chronic course, and by the constant excretion of sugar, diabetes mellitus is distinguished from those physiological and morbid conditions in which appreciable quantities of sugar appear in the urine *at times*—conditions which have, for the sake of distinction, been specially designated as *mellituria*, or *glycosuria*, although these terms are not always used strictly in this sense. On the other hand, the presence of sugar in the urine distinguishes diabetes mellitus from those affections in which an increased urinary secretion occurs as a primary or secondary symptom, such as *diabetes insipidus*, or *polyuria*.

The earliest reference to diabetes is found in the works of Celsus (lib. IV., cap. xx., § 2), who speaks of an inordinate increase of the urine, leading to emaciation and endangering life. Aretæus and Galen afterwards treated of the disease at greater length. The former first gave it the name of "diabetes,"—a word which seems to have been adopted even in his time, and which he derived from the transudation (*διαβαίνειν*) of the liquid ingesta and of the fluid constituents of the body into the urine (De causis diut., lib. II., cap. ii., and De morb. diut. curat., lib. II., cap. ii.), and referred the seat of the disease to the stomach. Galen held that the diuresis was a disease of the kidneys, which attracted to themselves the fluids drunk, and excreted them unchanged (De loc. affect., lib. VI., cap. iii., etc.). This view prevailed amongst almost all the later physicians of antiquity and of the middle ages, and even later, and is again met with, with trifling variations, in most of the writers who succeeded Galen; only a few maintain Aretæus's theory of an original affection of the stomach, or, like Zacutus Lusitanus, seek to combine the two theories. A wholly different interpretation of the disease was held by Paracelsus, who regarded it as the result of an abnormal formation of salt in the body, whereby the kidneys were stimulated to greater activity (De tartaro, lib. II., tract. III., cap. i.). His somewhat younger contemporary, Cardano, was the first to record comparative observations of the weight of the food and drink ingested and of the urine passed. Lastly, Sylvius, the founder of the iatrochemical school, regarded diabetes as the result of a morbid condition of the blood, as did Paracelsus, whom, however, he did not know, or at least does not mention (Opera med. Amstelodami, 1680, p. 724).

Up to this time—the middle of the seventeenth century—the whole medical world, at least in western countries, had no suspicion that the urine contained sugar, and it might, therefore, seem doubtful whether the affection previously described as "diabetes" was really diabetes mellitus, were it not that the statements in regard to the other symptoms, the result, and the prognosis, do not admit of a doubt that that disease was, in most instances, the one actually referred to, although in many other cases it was the far less dangerous simple or non-saccharine diabetes.

However, according to Christie (see Hirsch, l. c.), the Indian physicians seem to have been acquainted, from remote times, with a disease accompanied with sweet-tasting urine (honey-urine). All the rest of the world first learned of this peculiarity of the urine from the Englishman, Thomas Willis, in 1674. His discovery, although but little noticed by his contemporaries and immediate successors, gave an impetus to the division of diabetes into various forms, one of which is diabetes mellitus (the diabetes anglicus of Sauvages, the d. verus of other authors). But it was not until a hundred years later, when his countrymen, Dobson and Pole, and soon afterwards Home and Cowley, had shown sugar undoubtedly obtained from the urine, that diabetes mellitus was sharply defined as a special form of disease. About the same time, before the close of the eighteenth century, an immense advance was made by still another Englishman, John Rollo, who proved the injurious effect of vegetable food, which, in his opinion, was converted into sugar by an abnormal gastric secretion, and who introduced the absolute meat diet into the treatment of diabetes. This recognition of the different effects of vegetable and animal food was not without influence upon the theories of the disease. The old idea of a primary affection of the kidneys in diabetes was entirely given up, and from this time on attention was chiefly directed, on the other hand, to the function of digestion. For, although mention had before been made, at various times, of disorders of gastric and intestinal digestion, and of the action of the liver, yet these suggestions first found substantial support in Rollo's discovery, and afterwards were afforded greater scope by the advancing knowledge of digestion, particularly the conversion of starch into sugar within the alimentary canal.

The immense stride taken by chemistry in the beginning of the present century, and its application to medicine, were of no slight advantage to our knowledge of diabetes. The presence of sugar in the urine was now universally recognized and established beyond all doubt (P. Frank); observations upon the occurrence of sugar in the urine became frequent, and the reports of cases of diabetes, previously always somewhat meagre, increased markedly in number, thus rendering the symptomatology of the disease more complete. Finally, in 1835, after fruitless attempts by the most eminent chemists, Ambrosiani, the apothecary, succeeded in demonstrating positively the presence of sugar in the blood, previously conjectured by Dobson and others on account of its sweet taste, and by Rollo by reason of its diminished tendency to putrefaction. But, with all this, the essence of the disease was none the clearer; indeed, it was yet more mysterious in consequence of the multiplicity of the phenomena which men had learned to know, and of which autopsies even, with results for the most part negative, gave no solution at all. The theories which were brought forward, from about this time until towards the middle of this century, in regard to the nature of diabetes, all proceeded from the idea that the sugar originated in the system from vegetable food solely, whether primarily taken in as such, or formed out of starch by the influence of the digestive juices. Opinions differed only as to the reasons why the ingested hydro-carbons were not consumed, as normally occurs, but were excreted with the urine. Many referred the seat of the disease to the stomach, particularly Bouchardat, according to whose theory the starch ingested is transformed with unnatural rapidity into sugar by the action of a peculiar ferment existing in all diabetics, or, as he afterwards assumed, in only a certain class of them, is conveyed to the blood in abnormally large quantity, and therefore passes over into the urine. Mialhe sought for the fundamental disturbance in the blood, more particularly in its diminished alkalinity in consequence of suppressed perspiration, as a result of which the normal combustion of the sugar, which can take place only in the presence of free alkali, was interfered with. By this hypothesis he confirmed the efficacy of alkalies in diabetes. Others advanced less precisely expressed conjectures of disordered digestive or respiratory action, disturbances of the ganglionic system, etc.

Investigation took an entirely new direction when Claude Bernard astonished the world with his experiments upon the relations of the liver to sugar-formation (1848), and upon the excretion of sugar in the urine produced artificially by puncture of the medulla oblongata (1850), and by certain poisons (curare, 1854). Bernard, by showing how diabetes mellitus (not, indeed, the fully characterized disease in all its details, but yet its essential symptom, the excretion of sugar) could be produced, made this mysterious disease accessible to experiment, and pointed out the sources which would have to be investigated in the search for its origin. His pioneer experiments became the starting-point of numerous investigations, which indeed are not yet finished, but which yet have brought to light a store of facts in the physiology of sugar-formation, and of course have not failed to influence the pathology of diabetes mellitus. There are two prominent questions, the final solution of which is of the greatest importance to the pathology of diabetes, which up to the present moment form the subject of the most eager research. The one concerns the origin and purpose of glycogen in the system, that substance which stands in such close relation with sugar; the other is in regard to the nerve-tracts which govern the distribution of the glycogen and sugar. The views now held upon these questions, and their availability for the theory of diabetes, will be considered further on.

Etiology.

On the whole, diabetes is not a common disease; in fact, it was considered in ancient times, during the middle ages, and even up to the last century, as exceedingly rare, since even the most renowned medical writers possessed but a very meagre personal knowledge of it, or none at all. The disease is no longer so rarely encountered, perhaps from its having actually become more frequent in recent times, but perhaps, too, because more attention is paid to it and it is more easily recognized.

It occurs in all parts of the world, oftener, to be sure, in some regions than in others, but without appearing to be influenced by climatic conditions. According to statistical reports, diabetes mellitus seems to be particularly rare in Holland, Russia, Brazil, and the West Indies, and in certain localities entirely unknown. On the other hand, particular regions of India, and especially Ceylon, seemed even to the older physicians to be characterized by its greater frequency (see Hirsch, l. c.); in more recent times the frequency of diabetes in Thuringia has been specially remarkable, and it would seem also to occur more commonly in Wirtemberg than elsewhere (Betz, l. c.); in France it is most prevalent in Normandy, and in England in the agricultural counties, and mostly in the cooler ones, Norfolk, Suffolk, Berkshire, and Huntingdon (Dickinson).

I have succeeded in finding the following precise data in regard to morbility and mortality: In England, according to old reports, there occurred in the years 1848–1855, on an average, 420 deaths from diabetes annually, in an average population of 36,000,000, which amounts to a mortality of one in 86,000; in Ireland, in a population of over 8,000,000, 118 deaths—a mortality, then, of one in 68,000 (Hirsch, l. c., where there are further statistics of the mortality in certain towns, but without mention of the population). According to Dickinson, there occurred in England and Wales, in the ten years 1861–1870, one death from diabetes to every 3,509 inhabitants, and to every 632 deaths from all causes; and in Scotland, one to every 4,895 persons, and to every 916 deaths from all causes. In New York, according to G. M. Smith, during three years and a quarter, 58 deaths from diabetes occurred in a general mortality of 80,016 (0.07 per cent., then, of the total mortality).

According to Romberg,[1] of 10,000 patients at the Berlin Polyclinic, three were diabetic; in the years 1872 and 1874, according to the records of the Polyclinic, there were two cases of diabetes mellitus amongst 5,200 men, three amongst 5,450 women, and one amongst 5,900 children (besides two cases of diabetes insipidus in children)—altogether, then, six diabetics amongst 16,550 patients. In Greifswald, according to Ziemssen and Marmé,[2] there were three amongst 4,640 patients. In Würzburg, according to Gerhardt,[3] the reports of the Julius Hospital show seven diabetics amongst 4,460 patients in a period of three years. On the other hand, at the Jena Clinic, according to Ruickoldt, during ten years there were six diabetics to 3,853 patients, and in the four years following as many as seven to 1,300—in all, then, 13 diabetics to 5,153 patients.

It is to be noted, however, in regard to these figures from the clinics and polyclinics, that they probably give too low a relative frequency, since diabetes seems to occur more frequently amongst the well-to-do than amongst the poorer classes, to which these figures chiefly relate. Finally, it should be mentioned that, according to Seegen, diabetes mellitus is observed more frequently amongst the Jews than amongst Christians. Of his 140 patients 36 were Jews.

Although Prout says that diabetes does not occur in animals, it—diabetes mellitus as well as diabetes insipidus—is not rare amongst them; it occurs especially in horses, but in the other domestic animals as well.[4]

Heredity may be adduced as a predisposing cause in no small number of cases of diabetes. These are in part those cases in which several brothers and sisters, or even all the children of a certain family, become diabetic, and in part those in which one of the parents or grandparents has suffered with the disease and has transmitted the predisposition to the offspring; and it seems that an occurrence of this sort is not so very rare, at least that it is much more common than, until quite recently, we have been inclined to admit, for in recent times, since greater attention has been directed to the point, testimony in regard to the hereditary character of diabetes is constantly accumulating. Cases of the disease are sometimes met with even amongst the more distant relatives of diabetics.

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[1] Klin. Wahrnehmungen und Beobachtungen. Berlin, 1851. p. 115.

[2] Griefsw. med Beiträge, 1860 and 1861.

[3] Corresp.-Bl. des ärztl. Vereins von Thüringen. No. 11, 1874, p. 196.

[4] *Zundel*, Du diabète chez les animaux. See Virchow and Hirsch's Jahresbericht, 1872, I., p. 611.

Moreover, it is unmistakable that there is also a connection, due to hereditary predisposition, between diabetes and *diseases of the nervous system*, particularly *epilepsy* and *mental affections.* As this connection has not long been generally known, the cases in point are, to be sure, not yet very many in all; but they are positive and convincing enough, and continued research in this direction may be expected to furnish still further confirmation.

The first account of a case referred to heredity is to be found in Rondelet (see Salomon, l. c.), who observed the disease in a father and daughter; then Morton (see the same) tells of diabetes in a father and son, also of a case of a child, three of whose brothers and sisters had died of the disease. The statement that he had perfectly cured his three patients makes it doubtful, to be sure, whether they had really been affected with diabetes mellitus. Isenflaum mentions a family of eight children of parents who appeared entirely healthy, who, on reaching the age of eight to nine years, all fell victims to diabetes. Further examples are to be found in P. Frank, Blumenbach, Brisbane, Prout, Pavy, Dickinson, and others. I myself know of an instance in which two brothers were affected with the disease, and also of another from the Berlin University Polyclinic, in which four children of a Polish Jew were attacked with diabetes, and died of it. Marsh[1] tells, although not from personal observation, of a family in which the disease was transmitted even to the fourth generation.

The following figures will show that hereditary predisposition has been more noticeable, or rather has been more noticed, in recent times. Whilst Griesinger, in his collation of cases made in the year 1859, found in only three instances that the parents or fellow-children were diabetic, and knew of only two other cases in literature, Seegen alone had observed eight cases amongst 140 up to the year 1870, in which the father or the mother was diabetic, whilst in ten cases the fellow-children were affected, and in one instance the father had suffered from diabetes insipidus. R. Schmitz ascertained most positively the influence of heredity in 22 out of 104 cases observed from 1868 to 1874.

Langiewicz[2] found epilepsy in seven near blood relatives of a diabetic patient; one of Griesinger's patients had had epileptic seizures in childhood, and all the brothers and sisters had suffered, or were suffering, in the same way. Lockhart Clarke[3] met with diabetes mellitus in an epileptic who died of softening of the brain. Further data in regard to the coexistence of epilepsy, as well as of mental diseases (melancholia, etc.), are to be found in Seegen, Zimmer, Schmitz, and others.

Seegen and Betz even give cases in which man and wife were affected with diabetes mellitus, and the latter is inclined to regard this fact as an argument for the infectiousness of the disease. But, since actual infection has never been observed under circumstances more favorable thereto, it is much more reasonable to assume that, mere chance excepted, like causative conditions have been at work upon both husband and wife.

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[1] Dublin Quart. Jour. of Med. Sci. 1854. Vol. XVII., p. 17.

[2] De Diab. Mellito. Diss. Inaug. Breslau, 1850, p. 28.

[3] *Beale's* Archives of Medicine. Vol. IV. p. 146.

Diabetes mellitus occurs at every *period of life*—most commonly in middle age, far more rarely in children and the aged. It is particularly rare for the disease not to *develop* until old age, after the age of sixty or sixty-five, whilst it more frequently happens that it takes its rise in earlier years, and follows the patient to old age.

As regards *sex*, men are in general much more predisposed to diabetes mellitus than women are; but this holds good only for adults, not for children, with whom, as far as our present information goes, the female sex seems much more liable to be attacked.

Of Griesinger's 225 cases, 172 were in men and 53 in women; of Seegen's 140 patients, 100 were men and 40 women; of R. Schmitz's 104 patients, 77 were men and 27 women; of Zimmer's 62 patients, 49 were men and 13 women. Betz counted 24 men and 7 women; Leudet,[1] 24 men and 17 women; Andral, 52 men and 32 women; J. Mayer, 61 men and 13 women, etc. In England and Wales 4,273 men and 2,223 women died of diabetes from 1861 to 1870 (Dickinson). In general, the proportion of men to women is as 1 : 2 or 3.[2] According to observations at the Jena Clinic, however, the very reverse is the case in Thuringia, where there were only 3 men among 13 diabetics (see Ruickoldt and Gerhardt). Perhaps J. Vogel's statement, that the disease does not preponderate among men, may also be explained by local differences.

The occurrence of the disease in the different periods of life is shown in the following tabular arrangement, in which it is to be noted that in Griesinger's table the time of the *first appearance* of the disease is meant, so far as he could ascertain it from the literature, whilst in Dickinson's table *the age at death* is given, and that the other observers have recorded the patients' ages at the time of their first coming under observation.

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[1] Clinique Méd. de l'Hôpital de Rouen. Paris, 1874. p. 269.

[2] As 2 or 3 : 1 is probably meant.—TRANSLATOR.

	Griesinger.[1]				Seegen.		Schmitz.		Andral.		Mayer.			
	Males.		Females.								Males.		Females.	
		P. ct.		P. ct.		P. ct.		P. ct.		P. ct.		P. ct.		P. ct.
Up to 10 years..	3	1.8	3	5.8	0	..	1	0.96	2	2.4	0	..	0	..
10-20 " ..	22	13.3	14	26.9	5	3.6	8	7.7	3	3.6	1	1.6	1	7.7
20-30 " ..	42	25.5	14	26.9	23	16.4	9	8.6	12	14.3	3	5.0	0	..
30-40 " ..	49	29.7	11	21.1	21	15.0	16	15.4	20	23.7	8	13.1	2	15.4
40-50 " ..	31	18.8	5	9.6	33	23.6	16	15.4	20	23.7	22	36.1	4	30.8
50-60 " ..	11	6.7	3	5.8	43	30.7	38	36.5	13	15.5	19	31.1	3	23.1
60-70 " ..	5	3.0	2	3.8	14	10.0	12	11.5	12	14.3	6	9.8	3	23.1
70-80 " ..	2	1.2	0	..	1	0.7	4	3.8	2	2.4	2	3.3	0	..
	165		52		140		104		84		61		13	

Dickinson.[2]

	Males.		Females.	
		Per cent.		Per cent.
Up to the 5th year............	41	0.96	33	1.5
" " 10th "	62	1.5	52	2.3
" " 15th "	113	2.7	87	3.9
" " 20th "	221	5.2	131	5.9
" " 25th "	222	5.2	141	6.3
" " 35th "	651	15.2	368	16.6
" " 45th "	653	15.2	384	17.3
" " 55th "	746	17.5	352	15.8
" " 65th "	817	19.1	377	16.9
" " 75th "	594	13.9	236	10.6
" " 85th "	146	3.4	55	2.5
" " 95th "	7	0.16	7	0.3
	4,273		2,223	

The small percentage of children under ten years in Seegen's, Schmitz's, and Mayer's tables is explained by the fact that their observations were made almost exclusively in water-cure establishments; but in the other tables, too, the percentage seems to fall far short of the real facts, because in children the disease may so very easily be overlooked. Moreover, Dickinson's figures include diabetes mellitus and diabetes insipidus indiscriminately; but, since the latter is only very rarely fatal, it may be grouped with diabetes mellitus without any great inaccuracy.

It appears at once from the tables that in childhood, and up to the twentieth year of life, the female sex furnishes the greater proportion of diabetic patients.

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[1] In Griesinger's original the figures of percentage are incorrect throughout, being calculated somewhat differently from the above.

[2] The total of males in Dickinson's table does not agree with his statement of 4,271.

In quite recent times the number of cases observed in children has increased, and I find in literature twenty-eight *assured* cases in which the sex is stated (see Senator and Niedergesaess; also Ingerslev,[1] Schouboe,[2] Blackwell,[3] Hirschsprung, Budde, Schmitz, and E. Jacoby [4]). In addition, I know of the case of a boy twelve years old, and of that of a boy three years old, from the Berlin and Kiel University Polyclinics respectively, the latter having been communicated to me by Prof. Edlefsen. Of the whole thirty children under fifteen years old, eighteen were girls and twelve boys. The youngest child was a girl observed by Brown, who became ill at the age of twenty months, and died after a few months. I myself have observed a case of very late development of diabetes in a gentleman, who first noticed signs of the disease in his sixty-ninth year. Dickinson gives a case in which the disease was first developed in the seventy-first year.

Obesity, too, should perhaps be admitted as a predisposing cause; at least, well nourished and corpulent persons are attacked with diabetes with remarkable frequency, as Trousseau and Seegen have pointed out, and as Fleckles and Zimmer also have ascertained. In 52 of Seegen's 140, and in 18 of Zimmer's 62 cases, obesity had existed before the occurrence of diabetes.

Of the *exciting causes*, mention should first be made of *mechanical injuries*, to which the development of the disease was referred in a great number of well observed cases. Griesinger was able to record twenty cases of the sort, and Fischer[5] has collected seventeen, in which sugar appeared in the urine after an injury, accompanied in eight instances with other well-marked symptoms of diabetes. But their number has since been materially increased (see Kaemnitz et al.). It was for the most part concussions of the whole body, or of the brain and spinal cord in particular, which gave rise to the disease; more rarely, contusions of other parts, such as the liver or kidneys, by a blow or a fall, in which cases, for that matter, much more stress is to be laid upon the accompanying concussion of those nerve-plexuses or true vaso-motor centres seated in the abdomen. In such cases the disease has usually made its appearance a few hours or days after the infliction of the injury, rarely not until later—many weeks afterwards. In the latter event the injury has sometimes seemed to be only the mediate cause of the disease; a more profound structural change, such as tumor and the like, having in the meantime formed, in consequence of the injury, in the region of the nerve-centres concerned in sugar-formation.

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[1] Virchow and Hirsch's Jahresb. 1869. II. p. 262.

[2] London Medical Record. Nos. 59 and 60.

[3] Medical and Surgical Reporter. March, 1874, p. 234.

[4] See Virchow and Hirsch's Jahresb. 1874. II. p. 6.

[5] Arch. Gén. de Méd. XX. 1862. pp. 357 et seq.

Acute and chronic *diseases of the nerve-centres* come next in order, particularly those of the brain—inflammations, degenerations, and softenings, and, above all, tumors, which occasionally, as has already been mentioned, seem to have been first developed after an injury. The seat of these affections is mostly in the medulla oblongata or its immediate neighborhood, or, in case the special morbid focus is located further away, the region of the fourth ventricle is nevertheless in some way or another manifestly implicated, or else disturbances of its nutrition or circulation have resulted.

Furthermore, in not a few cases intense *psychical* impressions have proved the immediate occasion of the disease, or have aggravated it after temporary improvement had taken place—as well those of sudden occurrence, like fright, anxiety, or anger, as those of longer duration, like grief, solicitude, and care. Examples of this were known to T. Willis, and in subsequent literature they are found constantly repeated in great number, especially in times of stirring or shocking events. For instance, the period of engrossing stock-speculation in Berlin exerted an unmistakable influence upon the development or the aggravation of diabetes. Immoderate *mental strain*, too, is occasionally specified as the only ascertainable cause.

Errors in diet are frequently accused as predisposing or exciting causes, but with less certainty than those already mentioned—especially long-continued over-indulgence in farinaceous and saccharine food. Christie imputed the frequent occurrence of diabetes mellitus amongst the inhabitants of Ceylon to their almost exclusively vegetable and saccharine diet, and many would likewise refer the frequency of the disease in Thuringia to the quality of the food, which, amongst this largely agricultural population, consists chiefly of starchy materials. Several cases have been observed, too (by Griesinger, Zimmer, and others), in which persons who were excessively given to sweets, or who had suddenly changed their customary proper diet to a purely vegetable one, became affected with diabetes mellitus. But, in some of these cases, it is certain that other injurious influences have co-operated, such as a life of distress, emotional disturbances, the effects of cold, etc., whilst in others of them digestive derangements, preceding the diabetes for a long time, have resulted from the improper diet; and finally, the number of these cases altogether is so infinitesimal, in comparison with the vast consumption of starchy and saccharine articles of food, even in those nations which pre-eminently subsist upon them, that at least the immediate exciting influence of such a diet upon the development of the disease in general must appear questionable. Add to this that, neither in the human subject nor in animals fed on large quantities of sugar or starch for experimental purposes, has a true diabetes mellitus thus far been produced. But a *temporary* excretion of sugar in the urine may indeed be the consequence.[1] On the other hand, we may discern, in the comparatively slight nutritive value of a vegetable diet, in the necessity of eating large quantities of it in order to meet the demands of tissue-change, as well as in the digestive derangements frequently occasioned by the difficult digestibility of many vegetable substances, causes which may probably engender a *predisposition* to diabetes. In point of fact, in those very localities in which the greater part of the inhabitants live on coarse vegetable fare, and where at the same time diabetes is strikingly prevalent—as in Thuringia, for instance—diseases of the digestive apparatus, especially gastralgia, are also very common, more so than elsewhere (Gerhardt, Leube).

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[1] Thus *Vogel* states (p. 409) that, in healthy persons who had eaten 100 grammes or more of sugar within the space of a quarter or half an hour, he almost always found an unusual amount of sugar in the urine passed within from one to three hours afterwards. *Helfreich* also found sugar in the urine when the diet was exclusively vegetable, but not when it was exclusively animal. It is well known that in animals a temporary excretion of sugar may likewise be produced by injecting *large* quantities of sugar into the stomach or the portal vein, but no lasting diabetes. (See also "Theory of Diabetes.")

Berenger-Feraud has published an observation which seems to argue against, rather than for, the influence of a vegetable diet upon the development of diabetes (Comptes Rendus. 1864. I. p. 871). That is to say, he witnessed the occurrence of the disease in an ape, without any other cause than his having accustomed it to a miscellaneous diet, in order to protect it against tuberculosis upon transportation to a cooler climate. In this instance, too, it is likely that digestive disturbances, due to the altered diet, formed the connecting link between the feeding and the diabetes.

The very same holds good also in regard to *certain drinks*, such as new cider, wine, or beer, Weissbier, etc., after the immoderate drinking of which the disease has occasionally been seen to arise. These, too, are to be looked upon as at most only mediate or contributory causes. That cider-drinking, which was formerly freely accused, can have no direct influence, is proved by the fact that in England those districts in which a particularly large amount of cider is drunk show the smallest number of diabetics. *Exposure to cold and moisture*, whether on a single occasion or repeated and protracted, is not infrequently referred to as a cause. Griesinger found it alleged in 40 cases out of 152 in which the cause was specified, and he justly remarks "that, in view of the general misuse practised in speaking of this cause of disease, a good deal of caution is advisable in accepting it, but that it should not be wholly rejected as one of the efficient elements." In particular, we cannot set aside this cause in those cases in which a quite sudden outbreak of the disease follows close upon a thorough drenching of the whole body or of the feet, of which I find in literature several well observed instances (Zimmer, Kuelz, Oppolzer, Griesinger, et al.), and of which I have seen one myself. It appeared in a cab-driver, previously healthy, who, after having been wet through with the rain, fell ill with stomach symptoms, during the early days of which his great thirst attracted his attention. On examination, after about eight days' illness, sugar was found in his urine. In other cases the characteristic phenomena, thirst and increased secretion of urine, do not become noticeable until some weeks or even months after taking cold, following the previously indefinite complaints of weakness and pains in the limbs. In such cases the influence of the cold must always be doubtful.

Finally, many other circumstances are mentioned among the exciting causes, such as *severe bodily exertion*, *sexual excesses*, single gross *errors in diet*, etc. It is difficult, however, to prove their connection with the diabetes in any given case. Yet it is a noteworthy fact that diabetes is not infrequently developed, or at least makes its first appearance during *convalescence from febrile diseases of greater or less gravity;* in particular it is often seen to follow *intermittent fever*—at least ten times, for instance, amongst the 225 cases collected by Griesinger. According to the statements of Prout, Bence Jones, Rayer, and others, it would seem that gout also may induce diabetes.

Pathology.

General Description of the Disease.

Sometimes diabetes begins suddenly, but in general *very gradually*, with an increase of the urinary excretion and of thirst. Which one of the two is first increased cannot usually be established with certainty, although patients commonly first complain of the thirst, since it is the most troublesome symptom. The cases which begin suddenly are mostly those in which a manifest and definite cause, such as an injury or a severe emotion, has occurred, upon which, suddenly and after a very short interval, the quantity of urine and the desire for drink are strikingly increased.

In the far more numerous cases in which the disease is of more gradual development, the characteristic symptoms—increase of the urinary secretion and augmented thirst—are rather frequently preceded by certain phenomena which are regarded by many as *forerunners, or as the initial stage* of the diabetes. These are, on the one hand, *complaints referable to the digestive organs*—loss of appetite, nausea, and even vomiting, pyrosis, frequent eructations, irregular action of the bowels, and the like; and, on the other hand, *nervous derangements*, headache, sleeplessness, and even mental aberrations. It is uncertain whether all these phenomena should really be regarded as forerunners of the disease and not rather as exciting causes, or, indeed, as expressions of morbid processes, with which the diabetes stands in a more profound causative connection.

In the greater number of cases, however, either these premonitory symptoms are absent or they are not distinctly observed, so that the disease in its very beginning generally escapes observation, and is not remarked until it has become developed to a certain extent, when the patient's attention is attracted by a frequent desire to pass water, an habitual dryness of the mouth, or even an increasing debility or an impairment of sight, which leads him to seek medical aid, whereupon sugar is for the first time found in the urine and the diagnosis of the disease established.

Thus, in most cases it is really a matter of doubt, whether the urine contained sugar from the first, or whether this did not occur until after an increase of the urine and of the thirst—non-saccharine polyuria, or diabetes insipidus—had existed for a greater or less length of time. Perhaps a simple increase of the urinary secretion (diabetes insipidus) precedes the diabetes oftener than is commonly supposed, but is not noticed simply because patients seldom resort to the physician at the very beginning of their disease. But there are cases in which, exceptionally, the urine is examined very early, and the transition of diabetes insipidus into diabetes mellitus proved.[1]

The unusual *increase of the urinary secretion* and the extraordinary *thirst* often remain for a long time the only symptoms, but very burdensome ones to the patient. The urgent inclination to pass urine vexes him by day and repeatedly awakens him from sleep at night. As a rule, the *urine* is very pale and clear ; has not the peculiar smell of healthy urine, but a stale, or frequently an aromatic, wine-like odor ; and not infrequently leaves whitish spots of grape-sugar after it has dried upon the linen or the pot de chambre. *The thirst*, which goes hand in hand with the increase of the urine, harasses the patient still more than the frequent urination. Many patients may drink incredible quantities of liquid, and yet constantly complain of dryness of the mouth and throat. The secretion of saliva becomes scanty, the oral fluid grows thick and inclined to acidity, and even the teeth and gums become diseased.

The appetite also increases sooner or later, not infrequently to inappeasable hunger. But, although the patients eat much more than in their previous days of health, although they sometimes consume large quantities of food, the sense of satiety does not last long; after the heartiest meal they soon feel hungry again. Neither do they increase in size, weight, or strength; on the contrary, in spite of their abundant eating, *emaciation* is usually noticeable quite early; in particular, persons well supplied with subcutaneous fat often see this disappear in a very short time—in the course of a few weeks. With this is associated a constantly increasing *debility*, an inability to perform ordinary physical work. *Emotional derangement*, too, is commonly to be noted, and this is kept up and increased by the disturbance of rest at night. Many other *nervous phenomena* now not infrequently appear, if they were not already present at the beginning of the disease or before its definite onset—particularly pains in the head, sensations as of insects crawling over the skin, and of the limbs being "asleep," but also severe neuralgias, and finally very commonly *a decrease of the sexual instinct.*

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[1] See *Kuelz*, Beitr. I. p. 125.

The *skin* gradually becomes dry, harsh, and rough, and, if the emaciation be rapid, loose and flabby. The patients seldom or never sweat, but, on the contrary, are much inclined to shiver, and their skin often feels remarkably cool. Itching of the skin, too, is not uncommon, as well as furuncular and carbuncular inflammations, and even extensive gangrene.

In many patients the *breath* has a peculiar aromatic odor, like that of apples or fragrant hay, and at last the signs of chronic *pulmonary consumption* are very frequently developed, with slight fever at first, increasing subsequently.

Very common accompaniments of diabetes are *digestive disturbances*, and particularly diarrhœa; then *derangements of the sense of sight*, and more rarely of the other organs of special sense; and finally, signs of *kidney affections*, albuminuria, œdema, etc.

Rarely, and only in cases of the very briefest duration, do these symptoms progress uninterruptedly to the fatal end. As a rule, all the phenomena vary in severity for many months and even years, appearing sometimes graver and sometimes milder—even to complete disappearance; almost always in conformity with the state of the diuresis—becoming aggravated with its increase and ameliorated with its abatement. *Improvement and aggravation are chiefly dependent upon the sort of food taken*, unless the disease is already in a very advanced stage, with death close at hand. Farinaceous and saccharine food, and vegetable food in general, increases the quantity of the urine and the amount of sugar contained in it, and at the same time most of the patient's sufferings; exclusive abstinence from it, or even a diet in which albuminous, animal food simply preponderates, causes the symptoms to abate, and may indeed wholly repress them. The improvement thus obtained may be more or less lasting, and it may continue for a considerable length of time, even after the highly albuminous diet has been given up. In like manner as the vegetable dietary, but to a far lesser degree, emotional disturbances, excesses of any sort whatever, meteorological influences—in short, all those injurious agents which were specially mentioned, under the head of etiology, as exciting causes of the disease in general, may also exert an aggravating effect upon its course.

The influence of intercurrent febrile diseases upon the behavior of diabetes is very noteworthy. To a certain extent, namely, *all* of them diminish the saccharinity and the quantity of the urine, chiefly in consequence of the decrease in the amount of food taken and in the digestive activity resulting therefrom; but partly, also, because the sugar and water escape from the circulation by other channels than through the kidneys (by the intestine in diarrhœa, by exudations, and also, particularly the water, by increased cutaneous and pulmonary transpiration). But, apart from this easily comprehensible reduction of the amount and saccharine character of the urine, very striking variations are shown, which at present can scarcely be explained, namely, that during the continuance of the febrile affections the urinary symptoms sometimes entirely disappear, even when food is not wholly forbidden, and at other times they continue in considerable intensity. According to existing observations, it cannot be positively asserted that the variety of the febrile disease exerts an influence, but that in the case of certain diseases the effect is variable. Thus, according to Popoff, an attack of *relapsing fever*, for instance, had no effect at all upon the symptoms of diabetes, whilst Semon[1] relates an instance of the perfect abeyance of the latter as long as the former lasted. Leube witnessed a notable decrease in the excretion of sugar during a *pleuropneumonia*, whereas Petters saw no diminution at all, or only a very slight decrease, in *pleurisy*, *intermittent fever*, and *varioloid*. Other authors, again, have seen the sugar wholly disappear from the urine in *small-pox* (Rayer, Pavy, monograph, p. 109, de Carvalho[2]); but in this connection it is important to note that the variola always ended in death, which occurrence is in any case usually preceded by a disappearance of the sugar from the urine (see further on). *Typhoid fever*, whether ending in recovery (Pavy, l. c.) or in death (Griesinger,[3] Bamberger,[4] Gerhardt, l. c.), does not seem to arrest the secretion of sugar. Andral saw the sugar wholly disappear in febrile angina and in severe dysentery. Perhaps the diverse nature of the diabetes itself may explain the variations which are observed in instances of one and the same disease. (See also further on.)

Even the influence of the dietary upon the course of diabetes mellitus is not equally great in all cases, or indeed at all periods of a given case. In some cases, as was conjectured by Mor. Traube, but first actually ascertained clinically by S. Rosenstein, the morbid constitution of the urine, together with most of the other disturbances, is diminished very rapidly, and wholly disappears at times, if saccharine and starchy food be avoided. This occurs especially in well nourished, more or less fleshy persons, in whom the disease has developed quite gradually, and makes but slow progress. In others, again, generally those in whom the affection has broken out more or less suddenly, and has rapidly reached a certain height, the symptoms, particularly the excretion of sugar in the urine, persist, although perhaps less marked, even if the patients restrict themselves to a so-called "pure or absolute animal diet." On account of this diversity, many, like Bouchardat, Pavy, Harley, and notably

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[1] Zur Recurrens-Epidemie in Berlin. Inaug. Diss. 1873. p. 51.

[2] Phila. Med. Times. V. 1875. No. 169.

Arch der Heilk. III. 1862. p. 376.

[4] Würzb. med. Zeitschr. IV. 1863. p. 17.

Seegen, have assumed that there are two *forms* of diabetes, the one *mild* and the other *severe;* whilst others, like Mor. Traube, Bence Jones, and Dickinson, consider that there are not two separate forms, but only two *stages* of the disease, the mild form of the first-named authors being the first stage, and the severe form the second stage, into which the former may pass in course of time. It is really of little consequence whether we use the term "form" or "stage," only it seems as if, in establishing different "forms," a fundamental distinction would have to be made between those cases in which sugar is excreted only when vegetable food is taken, and those in which it is excreted during a meat diet — a difference which amounts to this: that in the one case the sugar proceeds only from the hydrocarbons ingested, whilst in the other it is derived from albumen also. Further on we shall have occasion to speak more fully of the sources of sugar in the organism; but we must here remark *that the formation of sugar or glycogen out of pure albumen* (*fibrine*, *white of egg*) *has not thus far been proved*, *but is yet quite doubtful*, *and that still less has any diabetic been observed to pass sugar while using a diet absolutely free from sugar and the elements which form sugar or glycogen; that is to say*, *a diet consisting only of albumen*, *the necessary salts*, *extractive matters*, *and drink.* A distinction between different "forms" of the disease cannot, therefore, properly be based upon the source of the sugar. The difference lies only in this: that some diabetics can retain and use up in their system more sugar and sugar-forming elements than others can, so that we may admit a gradation in this respect from the healthy man to the most marked diabetic. Even in health, too, there is a limit beyond which no sugar can be assimilated. (See further on, under "Theory of Diabetes.")

An additional reason for recognizing the different cases as different "forms," and not as different "stages," has been drawn from the fact that a change in their behavior under vegetable or animal food, *i. e.*, a conversion of the one "form" into the other, seldom or never occurs. This cannot well be disputed. It is generally granted that such conversions do really occur, in which patients who for a length of time have excreted sugar only when on vegetable diet subsequently do so even when on so-called meat diet. But it cannot be determined whether these are mere *exceptions*, and whether *most* other patients of the sort never throughout their whole life pass sugar so long as they restrict themselves to meat diet, because such an abstinence from vegetable food is scarcely ever continued for a term of years. It is *certain*, however, that the cases in which a strict animal diet, after having kept the disease in check for a long time, yet finally fails—cases, that is to say, in which a change, a conversion of the one kind into the other, actually occurs—do not indeed form an infinitesimally small minority; and it is *possible* that in such cases a previously mild course is transformed into a malignant one, no longer susceptible of being restrained even by a stringent diet.[1] Errors in diet, emotional disturbances, and causes of an unknown nature are, not so very rarely, the occasion of such a transformation. Moreover, Kuelz (Beitr. I. p. 217) has quite recently observed that a diabetic, in whom the proportion of sugar in the urine remained at times continuously at the same height, in spite of a restriction of the hydrocarbons, at other times passed urine free from sugar, even while taking sugar; whence it follows that patients with the so-called "severe form" may temporarily present the same phenomena as those with the "mild form." Kuelz has designated this as the "mixed form."

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[1] On account of the extremely protracted course of these benign cases, and by reason of the rarity of diabetes in general, it will readily be understood that it is but quite exceptionally that the opportunity is afforded to any one physician to observe the change in its behavior in respect to animal food. The physicians of the bathing-places to which diabetics mostly resort, who see a great many patients, seldom have the opportunity of observing the entire course of the disease. Moreover, *Seegen*, too, who most decidedly opposes the division into stages (monograph. 2d ed. p. 123), says: "Experience really teaches that a diabetes of this [milder] sort reappears in a severer form, in consequence of some unusual cause or another—generally emotional excitement; that even with entire abstinence from hydrocarbons the excretion of sugar continues, and therefore that the milder has given place to the severer form of diabetes." Amongst his observations, although but very few of them extended over a longer time than that spent at the bathing institute at Carlsbad, there is yet a considerable number which quite certainly show, in part, the transformation of the one form into the other (Nos. 16, 26, 34?, 43?, 45, 57, 76, 95, and 104). We find in *Griesinger* also a case in point (Arch. d. Heilk. 1860. p. 91), in which for a length of time the quantity of the urine, on a diet at no time absolutely animal (as it included salad and green vegetables), scarcely exceeded that of a healthy person, and the sugar constantly diminished (down to 0.1 per cent.!), but in which at length, in spite of the same diet, a fatal aggravation took place. Other cases are to be found in *Foster* (l. c p. 209, Case II. and Case XIV.). *Dickinson* also speaks of the transition of the one sort into the other, as of a settled matter. I myself had under observation a patient, who recently died, in whom, three or four years before, the sugar had disappeared from the urine as the result of strict diet, and appeared only as a trace even after the ingestion of small quantities of vegetables; whilst latterly 3.5 to 4 per cent. of sugar (80–100 grammes) appeared in the urine after an *absolute* animal diet of three or four days' duration.

From all this it appears that we cannot certainly determine beforehand how any case of diabetes will behave in its subsequent course, which fact forbids not only its division into sharply-defined "forms," but also the recognition of "stages" always following one another in definite sequence. Nevertheless, it is of great practical importance to know the influence of diet upon the course of the disease, and to test it in every case. Those cases which are brought to a standstill, at least for the time being, by curtailing the ingestion of hydrocarbons, as in the so-called meat diet, progress more slowly, of course, and the final phenomena, the dangerous and fatal complications, occur much later than in those cases in which the excretion of sugar cannot be overcome even by a rigid diet. The former are in every respect milder and more benign than the latter, but they may at any time become severe and malignant; and so, too, on the other hand, although far more rarely, an originally malignant case may, under favorable circumstances, pursue a milder course for a time, the ability to assimilate sugar and sugar-forming elements increasing.

Repeated attempts have been made to divide diabetes into various forms upon other grounds, particularly upon theoretical views as to its ultimate causes, all of which are more or less hypothetical, and thus far have been of no practical value. We shall return to these further on.

Under the name of *diabetes decipiens*, P. Frank has described a deviation from the ordinary features of diabetes, of not uncommon occurrence, and known before to Cowley, which consists in the urine containing sugar—and even a good deal of sugar—and yet the quantity of the urine being not much, if at all, above that of health—a state of things which may readily lead to errors in diagnosis. Here, too, so far as my own experience and my examination of literature extend, we have to do not with a special form always progressing in the same manner, but rather with a temporary decrease of the quantity of urine, without a corresponding diminution of the excretion of sugar. I am not aware of any case which has pursued its course, from beginning to end, with the urine containing sugar, but yet not increased in quantity. It happens, however, that with given amounts of sugar, unequally great, but yet abnormal, quantities of urine are evacuated; that during the course of the disease, either as the result of dietetic and therapeutic measures, or on account of large losses of water through other channels (the skin or the bowels), the amount of urine is diminished, whilst, on the other hand, that of the sugar does not decrease at all, or not in the same proportion.

On the other hand, it happens also that the saccharinity of the urine may be notably diminished, or wholly disappear for a longer or shorter period, whilst the quantity of the urine remains abnormally great.[1] In such cases also *inosite* has been observed to make its appearance in the urine in place of the grape-sugar (see further on).

Diabetes must be characterized as, in general, an incurable disease, since complete and permanent recovery occurs only exceptionally. The appearance of a lasting cure is commonly brought about by the excretion of sugar and the other morbid phenomena being kept in abeyance for a long time—not infrequently for years—by a judicious dietary; nay, many a patient regains his ability to eat vegetables in *moderate* quantity with impunity. But the slightest overstepping of these bounds, which would in nowise cause mellituria in a really healthy person, brings on the excretion of sugar again, and with it the other disturbances. We cannot speak, therefore, of a perfect, but only of a *conditional cure.*

In such patients, as a rule, the excretion of sugar finally gets the upper hand again, and *death* occurs in them only later than in those malignant cases in which the excretion of sugar cannot be repressed by animal food. The patients sometimes die suddenly, before the nutritive disturbances have yet reached a high grade, or even in the midst of a tolerably good state of health, in consequence of some trifling cause ; more commonly death follows after a more prolonged illness, and the patients succumb either to general exhaustion, without a discoverable affection of any organ whatever having taken place, or they die from the complications, of which pulmonary phthisis is by far the commonest. The cases of sudden death occur either under the guise of apoplexy with paralyses and loss of consciousness, or with peculiar phenomena resembling those of poisoning, of which we shall have more to say hereafter.

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[1] See, for example, *Ruickoldt*, Case 2; *Seegen*, l. c., p. 80; *Kuelz*, Beitr. I. p. 125 et seq., etc.

Pathological Anatomy and Chemistry.

There are no constant post-mortem appearances in diabetes mellitus. In many bodies, indeed, we find no striking visceral changes, at least none which can in any way be connected with the diabetes ; and even the microscope, which, it is true, has not very long been made use of in the investigation of the anatomical changes in diabetes, does not always reveal a textural change. In other cases, to be sure, the autopsy gives positive results : apart from casual and clearly intercurrent affections, some of these are to be looked upon as *secondary*, and as the results of the general disturbance of nutrition, of the increased loss of water by the kidneys, and the like—others do not admit of such an interpretation, and are on this account, or from the striking frequency of their occurrence, or, finally, from the physiological function of the affected organs, to be considered as *primary* changes, and to be associated in genetic connection with the abnormal formation of sugar. Amongst the secondary affections belong, for instance, the lung troubles which are so common in diabetics, as well as the not infrequent enlargement of the kidneys, and even inflammatory conditions of the same ; amongst the primary we may surely count certain affections of the brain, particularly in the region of the fourth ventricle, whilst in regard to most of the changes found in the digestive canal and its tributary glands it is doubtful whether they are causes or consequences of the diabetes, or whether they are co-ordinate with the latter in a common origin.

As a rule, especially if the disease has been of long duration and was not interrupted by sudden death, the cadaver shows a *high degree of emaciation;* upon the *skin* excoriations, ulcers, and gangrenous lesions are generally to be observed.

The *muscles* appear *dry*, withered and pale, but sometimes also rather of a dull reddish-brown color, as in cases which have ended rapidly with toxic symptoms. As regards the chemical condition of the muscles, our data relate only to their *containing creatine.* Gaethgens found 0.1988 per cent. of it in one case, and Perls[1] met with it in two cases, in which, however, the excretion of sugar had stopped before death, and the fluids and organs of the body were free from sugar, to the amount of 0.225 and 0.307 per cent. (with 1.363 and 1.689 per cent. of solid constituents). In addition, Perls found in the second case a small amount of creatinine. The amounts do not differ materially from the average in other diseases (about 0.256 per cent.).

As regards the internal organs, changes have been found rather frequently in the *brain*—partly gross and partly microscopic. Thus far, however, a special significance can be accorded only to changes of those portions by injury of which an artificial diabetes can be set up, chiefly, then, of the medulla oblongata, the fourth ventricle, and several parts of the cerebellum. Tumors (Levrat Perroton,[2] v. Recklinghausen, Richardson, Dompeling, Kratschmer, and others), extravasations of blood, and softenings (Lancereaux,[3] L. Clarke, Richardson, and Mosler), and, on microscopic examination, a wasting of the gray substance, degeneration and striking pigmentation of the ganglion-cells (Luys,[4] Martineau,[5] Zenker,[6] and Boettcher), and fatty degeneration of the vessels (Bischoff and others), have been found. H. Dickinson describes, as a constant lesion in diabetes and as the peculiar cause of it, a *dilatation of the arteries and of the perivascular spaces* in various parts of the brain and spinal cord, particularly in the medulla oblongata and in the pons Varolii, which would seem to lead to the escape of the contents of the vessels and to softening and destruction of the nerve-substance. According as death took place at an earlier or a later period of the disease, he found the arteries surrounded by more or less numerous altered extravasations of blood, which were gradually being absorbed, together with the remains of the destroyed nerve-elements, in place of which there were finally left lacunæ large enough even to be seen with the naked eye. W. Mueller,[1] however, has found this condition of the vessels in the bodies of non-diabetics also, and, on the other hand, has failed to find it in many diabetics. Kuelz, too, could not confirm Dickinson's statements (Beitr. I., p. 10).

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[1] Deutsches Archiv für klin. Med. VI. p. 243.

[2] Quelques considérations sur un cas de glycosurie, etc. Thèse. Paris, 1859. See *Trousseau*, l. c.

[3] Bull. de la soc. anat. 1860. p. 221.

[4] Comptes rendus des séances de la soc. de biol. Paris, 1861. II p. 29, and Gaz. méd. 1860-1861.

[5] Bull. de la soc. anat. 1861. p. 290.

[6] Schmidt's Jahrb. CXIV. p. 399.

In regard to the *spinal cord*, in other respects, there are but the most meagre and inadequate data. In one case G. W. Scharlau found it highly congested and softened, whilst other older authors speak of an induration of it. Dickinson mentions, as a very striking but not constant phenomenon, a dilatation of the central canal in the dorsal and lumbar portions, and a proliferation of the lining epithelium.

Changes are found in the *sympathetic nervous system* also, and especially in its abdominal portion, and probably they would be found oftener if they were always sought for carefully and with the aid of the microscope. Duncan[2] found the sympathetics in the abdomen from three to four times as thick as normal, and Percy[3] found the semilunar ganglion and the splanchnic nerves (besides the *vagus*) thickened and of cartilaginous hardness. In one case Klebs and Ph. Munk[4] were able to make out changes in the cœliac plexus, with destruction of a number of ganglion-cells; and so likewise did Lubimoff,[1] who found, together with sclerosis and atrophy of those cells, those of the inferior ganglion of the trunk of the vagus atrophied and abnormally rich in pigment. Finally, H. Henrat[2] once observed a tumor of the right vagus at the level of the root of the lung.

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[1] Beiträge zur pathol. Anatomie des Rückenmarks. Leipzig, 1871.

[2] Clinical Reports, 1818. Case 28, 137.

[3] Med. Gaz. 1842–1843. I. 49.

[4] Hand. der path. Anat. 3. 1870. p. 547, and Tagebl. der Innsbrucker Naturforscher-Vers. 1869. p. 113.

Affections of the *lungs*, and particularly chronic inflammatory processes leading to ulceration and phthisis, are very commonly found. The post-mortem appearances are given in sixty-four of the cases collected by Griesinger, and among these "tuberculosis" of the lungs was found thirty-one times, but in three instances it was cretaceous and obsolete. In eleven of the thirty-six cases in which a post-mortem examination was not made there also can be no doubt, from the symptoms described, of the presence of those affections of the lungs; so that "tuberculosis" was certainly present in forty-two out of a total of one hundred fatal cases. Dickinson found a still worse state of things, although, to be sure, the number of his autopsies of diabetics was far smaller. The lungs were found entirely healthy in only two out of twenty-seven patients who died in St. George's Hospital, infiltration and ulceration being met with in most of the others. According to Seegen, the lungs were found healthy only seven times among thirty diabetics who died in the Vienna General Hospital during the years 1838–1870, and whose bodies were examined; in all the others they showed pathological changes, and in particular one or both lungs were almost always infiltrated with tubercle and riddled with numerous cavities. Extensive *pneumonias* also and *pleuritic exudations* were present in certain cases, and finally *gangrene of the lung*, sometimes in conjunction with the other affections mentioned.

The *stomach* and the *intestinal canal* frequently show signs of a chronic catarrh, hyperæmia, thickening and tumefaction of their mucous membrane, and slaty pigmentation. Hemorrhagic erosions, too, are not infrequently present in the stomach, and dysenteric ulcers occasionally occur in the intestine (twice in the thirty cases cited by Seegen). The hypertrophic development may extend even to the muscular coat, particularly in the upper part of the digestive canal, as Dittrich (Leupoldt) has pointed out. It is worthy of remark, too, that, in consequence of peculiar chemical processes (the formation of acetone), the contents of the stomach often exhale an alcoholic odor (see Lambl, in Virchow's Arch. XI. p. 187).

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[1] Virchow's Archiv. LXI. p. 145.

[2] Bull. de la soc. méd. de Reims. 1874. No. 13.

It is only in recent times that particular attention has been paid to the condition of the *liver*, since Cl. Bernard's discovery of its share in the formation of sugar, although Richard Mead[1] had, full a hundred years before, pronounced diabetes a disease of the liver, the result of an unnatural concoction of the gall, and in support of this view had adduced the changes always found by him in the liver. This, indeed, is exaggerated, since in many cases we find no considerable change in the liver. In other cases, on the contrary, and by no means rare ones, it has been found *hyperæmic*, uniformly *enlarged*, and *hypertrophied*. In regard to the frequency of these changes, however, various statements are made, probably because the relative weight and size of the liver are subject to great fluctuations, even in a state of health, and therefore slight deviations easily escape recognition in a simple estimate by measurement with the eye, or are differently interpreted, according as the observer is more or less inclined to attach importance to the liver in diabetes. In the sixty-four histories of post-mortem examinations analyzed by Griesinger a considerable enlargement of the liver is given only three times, and slight enlargement ten times, among which there were a few instances of notable succulence and dusky, uniform hyperæmia. On the other hand, among the thirty diabetics examined after death at the Vienna Hospital, the liver was found enlarged in fifteen, gorged with blood, and hardened ; it was generally of a dusky-brown color, and in some cases its acini were less sharply defined or even obliterated (Seegen). Out of twenty-seven autopsies at St. George's Hospital, Dickinson found the liver healthy in only six cases ; in thirteen it was more or less hyperæmic; in three it was hard and enlarged, "without other change;" in four it was fatty; and in one case there was proliferation of the connective tissue (see further on). In a few cases the enlargement has reached the utmost degree. Thus, in a case published by Hiller,[1] the liver was enlarged to three times its natural size; in a case of Bernard's (Leçons. I. p. 416) to double size, weighing 2,500 grammes; in a case of Foster's, in a washer-woman twenty-seven years old, it weighed 2,110 grammes (circa sixty-six English ounces), and in a case of Dickinson's, with proliferation of the connective tissue, it weighed as much as nine English pounds and two ounces.

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[1] Opera Med. Gottingæ, 1748. Exposit. mechan. venenor. I. De Viperâ, p. 39: "Secti ex diabete mortui manifestum fecerunt ita rem esse. Semper inveni in hepate steatosi aliquid."

It is peculiar to diabetes, according to Klebs,[2] that the *congestion* of the liver depends upon an *active hyperæmia*. We see a faint rosy reddening diffused over the whole organ, and the individual acini, beneath the peritoneal coat as well as upon the cut surface, stand out as very sharply defined rosy spots, in which, on careful examination with a lens, we may recognize the capillaries, moderately dilated and highly distended, as an exceedingly close network of red lines. On the other hand, dilatation of the hepatic veins and their roots, such as occurs in static hyperæmia, is wanting; but, of course, the latter too may occur in diabetics, provided there be present causes of stagnation in the hepatic veins (in pulmonary affections, for instance).

But the *increased volume* of the organ depends in but slight degree upon the augmented quantity of blood contained in it, but to a far greater extent upon the *enlargement* of the *gland-cells*. Their contour is more rounded, their angles are less sharply defined, the protoplasm is abundant and slightly cloudy, and the nuclei are large and distinct. Upon the addition of a very weak solution of iodine, the whole cell (according to Rindfleisch,[3] however, only the nucleus) takes on a wine-red color; but remarkable variations may take place in the extent of this glycogenic reaction, which apparently depend in part upon post-mortem change of the glycogenic substance into sugar (Klebs).

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[1] Preuss. Vereinszeitung. 1843. p. 77.

[2] L. c. p. 378.

[3] Lehrbuch der pathol. Gewebelehre. III. Aufl. 1873. p. 412.

Moreover, according to Rindfleisch, there is a difference of behavior of the hepatic cells of any given acinus accordingly as they belong to one or another of its three vascular circuits. Only its *peripheral* portion, situated in the district of the portal vein, shows those changes, swelling and enlargement. The *central* part, in the territory of the radicles of the hepatic veins, is almost normal and allows that condition to be recognized at a mere glance; and finally, the *intermediate* portion, in the domain of the hepatic artery, is infiltrated with fat. Rindfleisch considers it uncertain, too, whether the enlargement of the cells in the tract of the portal vein proceeds from *genuine hypertrophy*. A growth and increased new formation of the hepatic cells, that is to say, a *hyperplasia*, seems likewise to take place in many cases, according to the statements of Stockvis and Frerichs,[1] who found, besides large and in part multinuclear cells, young cells and nuclei also. Both conditions, especially the hypertrophy of the cells, are perhaps to be explained by the increased ingestion of nutritive material so common in diabetics.

As a rule, the interstitial connective tissue does not share in the hypertrophy, although Trousseau records the occurrence of new formation of connective tissue with great enlargement of the organ (hypertrophic cirrhosis) in diabetes, and Dickinson, as has been mentioned, found the liver hard, enormously enlarged, and granular in one among twenty-seven cases. How far this change depends upon the diabetes is, of course, uncertain.

In the further progress of the diabetes, as Klebs states, the liver again diminishes in size, it becomes withered and flabby, and we no longer find the parenchymatous swelling of the cells so evident; often, indeed, fatty degeneration takes place. Perhaps Rindfleisch's statements rest upon such advanced cases; and probably, too, those exceptional cases (for instance, those of Fles,[2] Klebs,[3] Muench in Tscherinow, and Kussmaul's third case), in which a *diminished size* of the liver was found, with pigment-atrophy of the cells, are to be looked upon as final stages.

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[1] Klinik der Leberkrankheiten. II. Bd. 1861. p. 203.

[2] Donders' Archiv für holländ. Beitr. III.

[3] L. c., p. 538, case of Belke.

As regards *chemistry*, a *diminution of fat* in the liver has been observed in various quarters. Beale characterizes this decrease as a regular occurrence; Frerichs,[1] on microscopic examination in five cases of diabetes, found the hepatic cells wholly destitute of fat in four instances, and in one instance containing a slight amount of it; and on quantitative analysis Folwarczny found only 1.89 per cent. instead of the normal proportion of 2.5—3.3 per cent. (von Bibra). We must not expect, however, to find an abnormally small amount of fat in the liver in every case and in every stage of diabetes, since, on the one hand, fatty liver, depending upon infiltration, is present in many corpulent diabetics, at least at the outset of the disease, and, on the other hand, a fatty degeneration of the hepatic cells may supervene.

Amyloid degeneration of the liver, which has been found in some cases (Dutcher, Hartsen), is perhaps to be considered as the result of the cachexia and the pulmonary phthisis. Finally, the *formation of abscess*, found by Hartsen, and *obliteration of the portal vein*, by Andral in one instance, may be mentioned here as of occasional occurrence, on account of the importance of the liver in the pathology of diabetes.

The *gall-bladder* contains a small quantity of thickish bile. (As regards its chemical composition, see further on.)

Little is known in regard to changes of the *spleen*. It is generally described as enlarged, firm, rich in blood, and showing numerous follicles. (Compare Hiller, Klebs, l. c., p. 547; Kussmaul, cases 1 and 3.)

The behavior of the *pancreas* is in the highest degree remarkable. This organ, which, under other circumstances, is in general so rarely the seat of morbid changes, at least of the grosser sort, is found diseased with surprising frequency, in particular either simply *atrophied*, or, in addition, *degenerated*. Sometimes the degeneration consists merely in primary fatty destruction of the gland-cells, and sometimes it is induced by cancer, by the formation of calculi, and by obstruction of the efferent ducts, with cystic dilatation of the body of the gland. In certain cases the

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[2] L. c. I. Bd. 2 Aufl. 1861. p. 308.

wasting of the gland has reached the highest degree, so that scarcely any discernible remnant of the secreting parenchyma was to be found. The frequency of these affections of the pancreas was not noted until somewhat recently, in consequence of Bouchardat's contributions. Only isolated data in regard to this point have come down to us from earlier times, such as the discovery of calculi in the pancreas of a diabetic by Cowley, and that of cancer by Bright. Griesinger, who had found the pancreas atrophied in one of the five diabetics whose bodies he examined after death (in a maid-servant thirty-five years old; see Guenzler), still believed that this lesion was to be found in but a small minority of diabetics, and that it was of no significance whatever. But the observations which have since been published in great number (Hartsen, Fles, v. Recklinghausen, Frerichs, Klebs,[1] Harnack, Kuelz,[2] Schaper, and others) allow us to assume that diseases of the pancreas are present in about one-half of all the cases of diabetes. Among nine cases Frerichs[3] saw atrophy or fatty degeneration of the gland five times, and in the Vienna dead-house the pancreas was found strikingly small, soft, and anæmic in thirteen out of thirty diabetics (Seegen). It cannot be, then, that there is but an accidental coincidence; but a deeper connection must exist, and Klebs's view seems best founded, that the coexistence of diabetes mellitus and diseases of the pancreas depends upon lesions of the cœliac plexus. Either the disease (cancer, formation of calculus, and inflammation of the surrounding tissue) starts from the pancreas, encroaches upon the plexus, and gives rise to diabetes by destroying its ganglia (see "Theory"), or else the cœliac plexus is first affected, and in consequence thereof circulatory disturbances arise in the territory supplied by the cœliac artery, which lead to degeneration and atrophy of the pancreas.

The *kidneys* show morbid changes in the majority of cases: 32 times in the 64 autopsies collected by Griesinger; 20 times, according to Seegen, in the 30 cases at the Vienna dead-house: and, according to Dickinson, as many as 25 times in the 27 at St.

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[1] L. c. pp. 537 and 547.

[2] Beitr. I. Fall 3.

[3] L. c. I. p. 158.

George's Hospital. Ordinarily they are abnormally large, heavy, firm, and containing an abundance of blood, but without more profound textural changes—that is to say, in a condition of hyperæmia, which may, too, perhaps be associated with hypertrophy of the epithelium, and which may quite readily be understood as the result of the increased activity of the kidneys. In other cases the increased size of the kidneys no longer depends upon a simple hyperæmia and upon a hypertrophic swelling of the richly nourished epithelium ; but they are infiltrated with fat, and more especially in their cortical substance, which is consequently increased in thickness, and presents a dull, pale-yellowish aspect. Such kidneys, of course, contain an abnormal amount of fat, as, indeed, Beale has shown by quantitative analyses. Many authors look upon this change, which is probably but a result of the above-mentioned condition of hyperæmic swelling, as "Bright's disease of the kidneys," which they set down as a common complication of diabetes, especially if, as is not uncommon, the urine was albuminous during life (compare p. 904 et seq.). This interpretation is not correct, unless, indeed, we understand by Bright's disease all changes in the kidneys accompanied by albuminuria, and not merely the diffuse nephritis which leads to contraction. This latter affection occurs only exceptionally in diabetes, as is shown, on the one hand, by the state of the urine, and, on the other hand, by the fact that the granular atrophy, which is so common a termination of true "Bright's disease," is but very seldom met with in the bodies of diabetics.[1] Moreover, there are no known microscopical observations which have made out, in the enlarged kidneys so common in diabetes, the interstitial cell-infiltration and the new formation of connective tissue which are found in diffuse nephritis.

Catarrh of the pelvis of the kidney and of the ureters is rather frequently found. It may be caused in part by the final complications which prove fatal, and in part perhaps by the irritating effect of the sugar and other abnormal elements in the urine (q. v.). *Abscesses of the kidney*, found in some instances, also owe their existence probably to the same causes.

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[1] In the old accounts, which have come down to us from the period preceding the general knowledge of glycosuria, we often find mention of shrinking and destruction of the renal parenchyma. We may be allowed to conjecture that in these cases diabetes mellitus was confounded with contracted kidney, pyelitis, and hydronephrosis. (Compare "Diabetes Insipidus.")

Some other changes occasionally found in the kidneys are more remotely connected with the diabetes, such as *amyloid degeneration* (Dutcher, Seegen) and *tuberculosis* of the kidneys (Seegen), the occurrence of which is perhaps brought about by the pulmonary phthisis, which is so common.

As regards the *sexual organs*, there is nothing remarkable except *atrophy of the testes*, which has occasionally been observed in young patients (Romberg, Seegen, monogr. p. 114). The contents of the *seminal vesicles* have been examined in but few cases, and have then generally been found normal. In the case of a man forty-four years old, observed by Frerichs (l. c., p. 205), they contained a large quantity of gray fluid, with abundant spermatozoa, and a transparent ruby-red concretion as large as a pea.

In regard to the constitution of the *blood*, there is a lack of sufficient and trustworthy data. When death has occurred during the height of the disease, with toxic symptoms, it has been found abnormally thick and viscid (Kussmaul). This would correspond with certain old statements in regard to an abnormally high specific gravity of the blood-serum—as high as 1.033, for instance, according to H. Nasse and McGregor (the normal being 1.027–1.029). In other cases, on the contrary, the blood has not been found more deficient in water than normal, but even richer in it; thus, Bouchardat found 80.9 per cent., Henry and Soubeiran 81.6 per cent., Lecanu 84.8 per cent., and Simon 78.9 to 80.2 per cent., instead of the normal proportion of 78–79 per cent. of water. Probably the previous long illness, intercurrent diseases, great losses of water, and the like, have some effects upon these variations. Very frequently the blood shows quite a striking *abundance of fat*, and, on standing, a serum of a milky, chylous appearance separates, resembling an emulsion. This was noticed long ago by Dobson and Rollo, and has been confirmed by numerous subsequent observers, partly with blood taken from the cadaver, and partly with that obtained by venesection during life (Marsh, Hutchinson, Elliotson, Thomson, Siebert, Fuchs,[1] Pavy,[2] Hoppe-Seyler,[3] and Kussmaul). By agitation with ether it is possible to extract from such blood an appreciable quantity of fat. In three cases Simon found it in the proportion of 2–2.4 per cent., whilst the normal percentage is only 1.6–1.9.

The characteristic change in the blood is its being abnormally *charged with sugar*, which, since its discovery by Ambrosiani, has repeatedly been detected, and even subjected to quantitative analysis, although with very varying results, partly in consequence of the various and not always unexceptionable methods of investigation, but partly, too, because in an examination of cadaveric blood it may already have undergone metamorphosis in greater or less quantity. From the latter circumstance it also happens that occasionally no sugar at all is found in diabetic blood.

According to Corneliani, the sugar in the blood should amount to about one-eighth of that existing in the urine. Maitland found four grains of sugar in eight English ounces of blood, *i. e.*, 0.1 per cent., Fonberg[4] 0.034 per cent., C. G. Lehmann[5] never more than 0.047 per cent., Drummond 0.2 per cent., Rees 0.18 per cent., Pavy[6] 0.53 per cent., Gaethgens 0.2881 per cent. in the blood of the right side of the heart, but none in the arterial blood; and finally, Bock and Hoffmann 0.3–0.35 per cent. The latter, together with Pavy, who, as it appears, found the greatest proportions, examined the blood obtained by cupping during life.

Finally, too, in one case *acetone* was found in the blood by Petters (at least in the blood of the portal vein). From its presence in the urine (q. v.), and apparently also in the expired air, we may conclude that it may be present in the blood during life.

As in the blood, so, too, has *sugar* been found in most of the *organs*, *secretions*, and *exudations*, in which normally it occurs not at all, or only in very slight quantity: thus, besides the liver, in the brain (Vernois, Griesinger, Jaffé), in the inflamed lung (Grohe), in the spleen (Griesinger, Grohe), in the pancreas (Vernois), in the kidneys (Vernois, Grohe), in the testicles, in the muscular substance of the heart (Grohe), in the voluntary muscles (Griesinger, Gaethgens), and in the cerebro-spinal fluid (Bernard). The presence of sugar in exudations and dropsical effusions is of no special significance, unless very considerable in amount, since they frequently contain sugar even without diabetes ;[1] but, on the other hand, its presence in pus and purulent discharges is all the more remarkable (Pavy, Keller,[2] Francis[3]), since, according to Bock, in non-diabetics the sugar immediately disappears from the pathological fluids so soon as they become purulent. As regards the liver in particular, sometimes a striking amount of sugar is found in it (Cl. Bernard, Stockvis, Kuehne), and sometimes little or none at all. The latter need not be wondered at in those cases in which the phenomena of diabetes had disappeared a longer or shorter time before death ; but, even in other cases, the search for sugar may prove unsuccessful, on account of post-mortem transformation of the sugar (into lactic acid). The same is true of the *bile.* In diabetes artificially produced in animals it very rapidly becomes saccharine—more rapidly than the urine does (Cl. Bernard), which allows of the supposition that it is saccharine in the diabetes of man also.[4] Moreover, in the cadaver sugar may be diffused through the bile from the liver, but it may disappear again by further transformation.

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[1] See *Griesinger*, p. 366.

[2] Monograph, p. 105.

[3] Med.-chem. Untersuchungen. 4 Heft. Berlin, 1871. p. 551.

[4] Ann. der Chemie und Pharm. LXIII. 1847. p. 360.

[5] Lehrb. der phys. Chemie. II. p. 217.

[6] Monograph, p. 105.

Glycogen has been found in the brain, in the inflamed pia mater, in the inflamed lung, in the testicle, and in the spleen (Grohe, Jaffé), but, as Kuehne[5] has shown, its presence is independent of the diabetes. As glycogen is also found, under normal conditions, not merely in the liver, but in the muscles too, in smaller amount, nothing but quantitative analyses, with a comparison of its quantity in diabetes and in health, can be of any value. Such analyses cannot be carried out, since, as is well known, the conversion of glycogen into sugar takes place very rapidly in the cadaver. Grohe's statement, however, that glycogen has been found, although in small quantity, in the liver of a diabetic whose urine had contained 2.3 per cent. of sugar, is of importance in connection with certain theories of the nature of diabetes mellitus, since it justifies the conclusion that the liver of the diabetic did not cease to form glycogen during the disease. (Compare "Theory," further on.)

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[1] See *Bock*, in Reichert and du Bois-Reymond's Archives. 1873. p. 620.

[2] In Nasse's Unters. zur Physiol. und Pathol. I. p. 310.

[3] London Med. Gaz. Feb. 12, 1847.

[4] According to *Naunyn* (Archiv f. exp. Pathol. III. p. 167), the bile of rabbits and fowls naturally contains a small amount of sugar.

[5] Virchow's Archiv. XXXII. p. 536.

In regard to the changes in the other secretions and excretions, see below.

Special Symptomatology.

State of the Urinary and Sexual Apparatus.

The *increase in the quantity of the urine* is one of the earliest and most constant symptoms of diabetes, and is, as a rule, in direct proportion to the severity of the disease. In cases of moderate gravity the amount of urine passed in twenty-four hours varies between 2,000 and 5,000 cubic centimetres ; but larger quantities, up to six and eight litres daily, are nothing unusual, and now and then a still more copious excretion of urine is observed. I myself have several times seen the daily quantity exceed ten litres, and in one instance (in a man thirty-three years old) reach 12,200 c.c. ; Bence Jones saw it amount to seven gallons in a man, and Peter Frank even found it to exceed 52 lbs. ; but Fonseca's statement that a diabetic had voided 208 lbs. of urine in a day must rest upon an error.

Much more rarely the quantity of the urine is normal, or even abnormally small. The urine often contains a sensible amount of sugar, without its quantity, especially at the beginning of the disease, being notably increased—a condition which, as has been already mentioned (p. 878), P. Frank has designated as *diabetes decipiens*, but which, as has likewise been stated above, is always observed at times only, and never throughout the whole course of the disease. On the other hand, it is very common for the urine to diminish in quantity coincidently with the general subsidence of the diabetic phenomena, some time before the fatal termination. Intercurrent febrile affections likewise usually, but not always, diminish the amount of the urine and the other diabetic symptoms (see p. 874 et seq.).

Apart from these special circumstances, the amount of the urinary secretion is governed, in general, by the quantity of water ingested with the food and drink, rising and falling with the latter, but remaining, as a rule, somewhat below it. Exceptions to this occur, especially a urinary secretion notably less than the amount of water taken, when the system is losing large quantities of water by unusual channels, as in diarrhœa, the profuse perspiration of febrile diseases, etc. The reverse of this—an excess of the amount of urine over that of the water drunk and taken with the solid food—takes place more rarely, as when, according to Griesinger, the patient cannot drink in proportion to his thirst; but it may happen apart from this, as appears from Gaethgens' investigation, for example, but certainly not so frequently as the older observers assumed on the strength of mere appearances. In such a case, the excess of water evacuated in the urine, as well as in other ways, as by perspiration and defecation, must of course be furnished from the store of water present in the body, and from the water newly formed by the oxidation of the ingested hydrogen. It has often been maintained that the urinary evacuation in diabetics is greater *at night* than *by day.* This is in nowise shown by the observations at our command, since, on the one hand, the very reverse, namely, a greater evacuation of urine by day, has been noticed in several thoroughly observed cases (see, for example, Limann, Ott, and Kuelz); and, on the other hand, the observations of Petters, Ott, Leube, and Kraussold, which would seem to support that assertion, were made under very unlike conditions, so that they do not in any wise warrant a generalization of the results thus arrived at—nay, some of them rather point to the opposite conclusion.[1] So many individual differences come into play—habits, soundness of sleep, diet, and numerous other collateral circumstances—that a uniform behavior under all conditions is not to be thought of. One point of difference between the behavior of the urinary excretion in a healthy person and in a diabetic was first shown by C. Ph. Falck, and confirmed by Neuschler and Kuelz; it consists in this, that the increase in the quantity of the urine after taking water occurs much more slowly in diabetics than in the healthy. Falck explained this fact by a retardation of the absorption of water in the intestine; but J. Vogel has given another explanation, in consonance with his theory of diabetes. (See "Theory.")

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[1] Thus, for example, "day" and "night" are used in quite different senses by the different authors. Ott reckons the night from 10 o'clock in the evening to 10 o'clock in the morning, Leube from 6 P.M. to 6 A.M., and Kraussold from 7 P.M. to 7 A.M. Ott's patient took coffee, etc., at 7 A.M., that is to say, during the "night;" rose

In proportion as the urine increases in quantity, its *color* becomes lighter, owing to dilution of the coloring matter. Even with a moderate increase of the secretion, the urine has an abnormally light color, verging on greenish, and with a greater increase, especially in thin layers, it looks almost entirely colorless and as clear as water. It is also a result of the high proportion of water, that diabetic urine is almost always *clear* and *free from the sediments* which form in urine deficient in water, by precipitation of the somewhat insoluble uric acid and its salts. If the quantity of the urine becomes diminished from any of the above-mentioned causes, or in consequence of a temporary improvement in the disease, free play is again given to the formation of sediments. On standing for a length of time, particularly in a warm place, saccharine urine becomes turbid from the development of fermentation-fungi.

The *odor* of the urine, in the course of a few hours, if not immediately after its evacuation, is very often peculiarly aromatic, likened by the older physicians to that of hay. According to recent observations, the causes of this are to be found in acetone and alcohol. If the urine is very highly saccharine, it may have a sweet *taste;* but nowadays, with our trustworthy

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between nine and ten—in the "night" again, etc. That the patients of the different observers took their food, especially the evening meal, at various times—one while it was still "day," and another when it was already "night;" that their mode of life in other respects, as exercise and rest, was very unlike; and much else in addition—should likewise not be left out of account.

and convenient methods of detecting sugar, this test is of no value at all.

The *reaction* of the urine is not only acid while it is fresh, but it remains so much longer than it generally does in healthy urine, and especially that which is very watery. This is occasioned by the formation of acid in connection with the fermentation of the sugar. Montegazza's statement, that it does not become alkaline even after the prolonged use of bicarbonate of soda, I do not find confirmed.

Saccharine urine always has an unnaturally high *specific gravity*, which, while due to the contained sugar, is not necessarily in precise proportion to it, since the other solid constituents of urine have some, although much lighter, influence upon its weight. At an early period the specific gravity exceeds the physiological limits (1.020–1.025), and very commonly rises to 1.035 or 1.040, nay, even to 1.060. Bouchardat observed a specific gravity as high as 1.074. Exceptionally, in weakly patients or those who are very much enfeebled, we may find the urine saccharine indeed, but yet of natural, or even abnormally low, specific gravity, probably because a portion of the sugar has already undergone fermentation, while the other solid constituents (urea, salts, etc.) are so small in amount that the sugar still present does not suffice to raise the weight. The quite exceptional observations of Pavy, who once found a specific gravity of 1.010, and of Dickinson, who saw it fall as low as 1.008, are probably to be explained in this way.

The sugar, which forms the characteristic element of the urine, is *grape sugar* (starch- or amorphous (Krümelzucker) sugar, glucose, or dextrose), distinguished by its ready solubility in water and alcohol, by its rotating the plane of polarization to the right, and by its capacity for fermentation. Its quantity varies widely in different cases, and at different times in one and the same patient. The proportion of sugar to urine may range from slight, but still perceptible traces up to 10 and even 14 per cent., according to Vauquelin and Ségalas and Lehmann; and accordingly the amount excreted daily will vary from a few grammes to a kilogramme and over. The highest quantity in twenty-four hours, carefully examined, seems to have been observed by Dickinson in a man twenty-five years old, who voided fifty English ounces of sugar (about 1,500 grammes). As a rule, however, the daily evacuation does not exceed, for any considerable length of time, 200 or 300 grammes, rising higher only in very severe and advanced cases.

For the most part the absolute amount of sugar excreted in the urine keeps pace with the excretion of water, so that, in general, more sugar is excreted when the urine is abundant than when it is scanty, and *vice versâ*. Hence, whatever affects the quantity of the *urine* usually affects that of the *sugar* in the same direction. Exceptions to this occur, however, especially during short spaces of time, as in the various periods of the day, depending, as a rule, upon the quality and quantity of the solid food taken. Food containing starch or sugar, for example, increases the excretion of sugar in every case and very speedily, and, if a good deal of fluid be not taken at the same time, in greater proportion than it does the excretion of water. The influence of the sugar and starchy matters ingested is manifested in so short a time as half an hour (Kuelz, Beitr. I., p. 122), and may be at an end in from four to six hours, although it commonly lasts longer. Thus, it may happen that the sugar may wholly disappear at a time long after a meal, as was remarked by Bouchardat in 1839, by Baudrimont,[1] and by others—a course which is very often observed in the beginning of the disease or in slight cases. Under an exclusively animal diet, on the other hand, the variations occasioned by the meals are less pronounced, probably because with this diet the formation of sugar is not so rapid and abundant, and therefore its excretion takes place more gradually and slowly. It has already been mentioned that, in mild cases or in the early stage, the excretion of sugar, together usually with the other morbid phenomena, may be made to disappear entirely by animal diet. Finally, it must be added that, as stated by Bouchardat and recently confirmed by Kuelz, the sugar in the urine and other secretions may decrease in quantity and wholly disappear for the time being under the influence of muscular movements.

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[1] Comptes rendus. XLI. p. 176.

Urea is almost always excreted in abnormally large amount by diabetics, as any one may easily convince himself in every case. The quantity voided in twenty-four hours may amount to twice or thrice the normal, so that in adults a discharge of 100 grammes and even more (142 grammes in a case of Dickinson's) has repeatedly been ascertained. The greatest increase in the quantity of urea observed by myself (see Niedergesaess, Inaug. Diss.) occurred in a girl twelve years old, weighing at the outset 20.5 and afterwards 17 kilogrammes, who passed daily 54.05, 51.33, and on one occasion 69.92 grammes of urea, together with 353, 475, and 570 grammes of sugar; whereas, under ordinary circumstances, children of that age excrete only about 14 grammes of urea—an increase, therefore, to nearly *five times* the normal! The earlier statements of Berzelius, Prout, and E. Schmid, that the urea is diminished in diabetes, or that it is not present in the urine at all, either rest upon defective methods of investigation, or else refer to the *percentage* of urea contained in the urine, which is, to be sure, abnormally small in proportion to its great abundance of water; or, finally, they were owing to special circumstances which did not warrant any conclusion in regard to the usual state of things in diabetes, as, for instance, the examination of the urine of very reduced patients who were near their end, and the like.

The increased excretion of urea depends primarily upon the large quantities of food taken to appease the hunger, and especially upon the highly albuminous food which patients take, upon medical advice, indeed, as a rule. An additional reason, however, is to be sought for in the increase of the liquids ingested and of the urine excreted; for it is well known that the quantity of urea is thus increased, partly because it is more thoroughly washed out of the tissues, partly because it is formed in augmented quantity, rising, as appears from the researches of Boecker, Genth, Kaupp, Mosler, and Voit, at the average rate of about 0.3 or 0.4 gramme for every 100 grammes of urinary water. It was shown, however, by the comparative researches of Reich, Gaethgens, Pettenkofer, and Voit, that diabetics, even upon a highly nitrogenous diet, did not thereby gain in weight by assimilating the nitrogenous material as did healthy persons living under the same external conditions, but they voided with the urine more azote than the latter and more than corresponded with the ingesta, even if they drank no more water and passed no more, or but little more, urine than the persons with whom they were compared. Hence, it follows that in these diabetics there was an increased metamorphosis of nitrogen peculiar to the disease and independent of the two first-mentioned causes. Since this increase was positively ascertained, it has been regarded by many as a process taking place in all diabetics without exception, and the very essence of the disease has been sought for in *increased decomposition of albumen* into urea and sugar, not occasioned by external causes, but taking place specifically at the expense of the body itself. But, without limitation, this is not correct. The cases in which the excretion of urea was ascertained as not to be explained by the greatly augmented ingestion of food and excretion of urine, were, as appears from the high excretion of sugar and from the accompanying data, very severe from the beginning or very far advanced cases of diabetes, such as, it is in the highest degree probable, would still have gone on excreting sugar even with a protracted exclusion of hydrocarbons from the diet. Direct observations in regard to this, extending over several days, were not made in the cases in question. For such cases, or for the majority of them, the assumption of an increased destruction of the albumen of the body is indeed correct, although, even in these cases, loss of weight may be avoided, at least for the time being, by an inordinate consumption of meat and fat (compare Pettenkofer and Voit, Vers. VIII and IX). For milder cases, on the other hand, or for a case in the earlier stage, for one in which no sugar is excreted while exclusively animal diet is used, an excessive loss of urea, independent of the diet and of the heightened diuresis, has not been shown and is very improbable. In patients of this sort the increase in the loss of urea does not generally reach a high degree, but is kept within moderate bounds, and in such cases, at all events, the increased ingestion of albuminates and water will suffice to explain the augmented discharge of urea until the contrary has been proved by adequate investigations into the metamorphosis of elements in such diabetics. The very fact that in them the exclusion of the hydrocarbons from the food puts a stop to the excretion of sugar, makes rather against than in favor of a specific increase of the destruction of albumen.[1]

In accordance with the theory of a decomposition of albumen into urea and sugar, we ought to find a definite relation between the quantities of the two substances excreted in the urine. Such, however, is not the case, least of all in those cases in which, together with albumen, variable amounts of sugar or starch are taken with the food, which immediately increase the excretion of sugar. Neither can we reasonably expect it by deducting from the excretion the amount of sugar or starch eaten, or if the excretion of sugar takes place merely at the expense of the other constituents of the food or of the body, and for just this simple reason, that the whole amount of sugar and urea do not enter the urine as fast as they are formed, but in different proportions. Sensible quantities of sugar enter into most of the secretions, transudations, and exudations, whilst urea gains entrance to but very few of them, and then generally only in traces. Besides, it is certain that even in diabetics not all the sugar taken into the body or formed therein is excreted without having been made use of, but is consumed—sometimes more of it and sometimes less; and so on this account we cannot say that there is an invariable relation between the excretion of sugar and that of urea.

Neither is there any constant relation between the amount of *urinary water* and that of urea, for the quantity of the latter is chiefly governed by the proportion of nitrogen in the food, and in particular is notably increased by a highly albuminous diet, which so commonly lowers the quantity of sugar and water in the urine.

In diabetes, as in many other diseases, a febrile condition increases the amount of urea (Gaethgens).

Uric acid is probably always present in diabetic urine, although it frequently cannot be recognized by the methods ordinarily employed (precipitation by muriatic acid), because it remains wholly or in great part dissolved in the watery urine, and perhaps also on account of certain peculiar conditions of admixture which interfere with its precipitation. According to Naunyn and Riess and Kuelz, it is possible by other methods, as, for instance, by precipitation of the urine with acetate of mercury after it has been filtered through precipitated sugar of lead, to recognize the uric acid; but the quantities thus found, never exceeding 0.7 or 0.8 gramme, are usually somewhat below the normal, especially if we take into account the increased evacuation of urea with which, under other circumstances, that of uric acid ordinarily goes hand in hand. If the urine be concentrated, as it is in many cases at the beginning of the disease or during a temporary improvement, the uric acid is not only easily precipitated by the addition of muriatic acid, but it often shows itself on the mere cooling of the urine, and that in greater quantity by reason of the acidity being more marked in saccharine than in normal urine. In this sense we may assent to the remark of Prout and others, that the occurrence of uric acid sediments is of favorable import.

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[1] *Jeanneret* (*Naunyn*) observed, in a dog poisoned with carbonic oxide, sugar in the urine and an increase of urea, which was not to be explained by the augmented secretion of urine alone. But the disturbances caused by carbonic oxide are too manifold and far-reaching for this experiment to be esteemed conclusive.

Febrile conditions increase the amount of uric acid, as well as that of urea (Gaethgens).

Hippuric acid has been detected in diabetic urine by Lehmann,[1] Ambrosiani, Simon, Huenefeld, and Duchek, and, it is said, in greater quantity than in normal urine; indeed, W. Wicke[2] recognized it on the mere addition of muriatic acid to the diabetic urine. As a certain vegetable diet considerably increases the excretion of hippuric acid, and as a specially animal diet lowers it, we must await further investigations with special reference to the diet and to the substances, such as benzoic and chinic acids, which may happen to favor the formation of hippuric acid, before coming to a conclusion in regard to its actual variations in diabetes.

Winogradoff, Stopczanski, Gaethgens, and K. B. Hofmann[3] could find but very small quantities of creatinine, or none at all, in the urine. This, as I venture to assume after numerous examinations of my own, was chiefly owing to the method employed by them for its detection, which gives too small an amount of creatinine in diabetic urine. By a modification of it I have been able to detect a normal and even an abnormally high excretion of creatinine—as much as 1.43 and 1.86 grammes in twenty-four hours.[1] In other cases, it is true, I too have found relatively low proportions, but probably this was the fault of the method, which cannot always be carried out with quite enough uniformity. If, in a portion of the cases of diabetes, the excretion of creatinine shall actually be found diminished, the fact would be in the highest degree remarkable, and at present inexplicable, taken in connection with the circumstance that the diet of diabetics—who eat a good deal of meat, which chiefly affects the amount of the excretion of creatinine—is precisely the one which is very rich in creatinine (or in creatine), as well as with the fact that, according to the observations which are at hand in regard to the matter (see above, p. 881), their muscles are not also abnormally deficient in it. In regard to the condition of the nervous tissue (brain), in which, next to the muscles, the largest amount of creatine is found in health, no observations have been made.

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[1] Diss. de urinâ diabeticâ. Lipsiæ, 1835.

[2] Zeitschr. f. rat. Med. N. F VII. p. 311.

[3] Virchow's Archiv. XLVIII. p. 358.

In common with other nitrogenous constituents, creatinine also is excreted in increased quantity during febrile conditions, according to Gaethgens.

Of the inorganic constituents of the urine, *sulphuric* and *phosphoric acids*, being chiefly produced by the decomposition of albuminates, are generally proportionate to the *urea*, and are, therefore, like the latter, usually somewhat increased. On account of the small daily excretions which are to be considered, the variations are not always very striking; but with a very abundant meat diet quite considerable quantities are sometimes observed—double or triple the normal. Thus Parkes found a daily excretion of 4.19 and 5.4 grammes of *sulphuric acid*, instead of the normal amount of 2–2.5 grammes; and phosphoric acid, which, under ordinary circumstances, is excreted to the average amount of 3.5 grammes, has repeatedly been seen to reach 5 grammes, and even more, indeed, in a few cases; thus, Seegen speaks of 6.6 grammes, and Houghton of as much as 13 grammes.

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[1] I shall shortly contribute the details upon this point in Virchow's Archiv.

The excretion of *chlorine* (as chloride of sodium) depends almost altogether upon its ingestion in the food, and therefore, on account of the increased appetite, it too is augmented as a rule. Perhaps, also, the heightened secretion of urine exerts some influence upon this increase, since, according to Boecker, Genth, Kaupp, and Mosler, for each additional 100 cubic centimetres of urinary water 0.22 gramme more salt is excreted on an average. Possibly we may thus explain why Gaethgens observed in his patient a somewhat greater daily excretion of salt (15.43 grammes) than in himself (13.01), under quite the same dietetic conditions, unless some special circumstances, such as the loss by perspiration, etc., came into play.

As regards the behavior of the bases present in the urine, in the first place the *alkaline earths*, in combination with phosphoric acid, have been found in abnormally great amount by various observers. Thus Neubauer[1] saw in the urine of a diabetic child six years old, as the mean of nine days, a daily excretion of 0.711 gramme of phosphate of lime (about double the normal quantity for an *adult*), and 0.388 gramme of phosphate of magnesia (the normal amount in the *adult* being about 0.6 gramme). Boecker found, in an adult diabetic, 4.239 grammes of the two salts together; Benecke,[2] 1.11 grammes of phosphate of lime and 1.72 grammes of phosphate of magnesia; J. Vogel, the enormous quantity of more than 30 grammes of lime in one day (perhaps in consequence of an abnormal ingestion of lime?); and Gaethgens, 0.954 gramme of phosphate of lime and 0.599 of phosphate of magnesia, whilst a healthy person, under like circumstances, excretes daily only between 0.801 and 0.417. Finally, Dickinson found, in a woman thirty-five years old, while not upon an exclusively animal diet, an average of 2.76 grammes of lime as the mean of two days—from nine to ten times the normal amount; and, while upon a strict meat diet, 3.19 and 3.38 grammes, together with 0.52 gramme of magnesia (about double the normal); in other cases the increase of the two bases was less considerable, and in still others their excretion did not exceed the normal, although it was impossible to discover the causes of these variations in the diet or in an extraordinary ingestion of those alkaline earths. Dickinson supposes that a heightened excretion of lime takes place in those cases in which there are profound changes in the nervous system, and seeks to explain it by the large amount of phosphoric acid which is set free by the destruction of nerve-tissue, acting as a solvent upon the lime in the organism, and thus effecting its excretion.

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[1] Journal f. pract. Chemie. LXVII. p. 65.

[2] Zur Physiol. und Pathol. des phosphors. und oxals. Kalks. 2 Beitrag. Göttingen, 1850, p. 19.

There are but very scanty data in regard to the peculiar alkalies of the urine. It follows, from what has been said about the excretion of *chlorine*, that these, and more particularly the sodium, are usually excreted in increased amount. Gaethgens also found more alkalies, in combination with *phosphoric acid*, in the diabetic than in the healthy person. Dickinson did not find the alkaline salts increased.

Abnormal constituents, apart from sugar, are not infrequently found in diabetic urine, and, above all, *albumen*. The data in regard to the frequency of its presence are very various, perhaps on account of its not always being sought for, perhaps also because in many cases it appears only at times. Garrod found albumen in 10 per cent. of all cases, and v. Dusch in 28.5 per cent. Smoler observed it in one out of six cases, and I myself in two out of sixteen cases, some of which were under prolonged observation, and others seen but casually. The percentage of albumen is almost always very slight so long as the quantity of the urine is markedly increased, and on account of that increase.

Formerly, and even up to the most recent time, this, as well as almost every albuminuria, was considered as a symptom of "Bright's disease of the kidneys." The state of the urine is indeed suggestive of contracted kidneys, in which likewise a pale, clear, slightly albuminous urine is commonly voided in large quantities. But, as has already been mentioned while speaking of the post-mortem appearances, contracted kidney is found only exceptionally in diabetes mellitus, and, moreover, in most of the accounts which mention the albuminuria of diabetics, we look in vain for those conditions in the urine which are found in the stages of nephritis which so commonly precede the contracted kidney, as well as for other signs to warrant the diagnosis. As a rule—and such was the case, too, in both the cases observed by me—the urine contains no morphological elements whatever, neither red nor white blood (or pus) corpuscles, nor epithelium or their detritus, nor casts; as a rule, too, there is no hypertrophy of the heart. There is, then, nothing to justify the assumption that the albuminuria, which is one of *the commonest* occurrences in diabetes, is occasioned by diffuse nephritis, although it cannot be denied that the latter may supervene as an exceptional complication. The same is true also of amyloid degeneration of the kidneys, in which likewise the urine is observed to be similar to what has been described, although generally richer in albumen.[1] This, too, is but very rarely found in diabetes mellitus—much more seldom, at all events, than albuminuria; and besides, we should only quite exceptionally dare venture to diagnosticate it, in case of very advanced pulmonary phthisis, with involvement of other organs. No more should we suspect static hyperæmia of the kidneys and its sequelæ, which, to be sure, likewise lead to the evacuation of albumen in the urine; for in them the renal secretion differs entirely from that of diabetes. Dropsical effusions, particularly anasarca, which, as a rule, belongs to each of the three renal affections named, are very rare in diabetes mellitus, even when albuminuria is present. It is not until the derangement of nutrition has reached the highest degree, and death by marasmus is impending, that œdema makes its appearance in the lower limbs.

We must therefore assume that the albuminuria now under consideration does not depend upon any profound textural change in the kidneys, but upon some process less grave, and capable of retrogression under certain circumstances, in consequence of which either the transition of albumen from the blood into the urine is favored, in which case an abnormal condition of diffusion is present, or else the epithelium becomes incapable of assimilating the albuminous nutritive material which reaches it. It is not likely that the escape of albumen is in any wise occasioned by the saccharinity of the blood flowing through the renal vessels, because in the majority of cases of diabetes there is no albuminuria, and because the latter, as has already been mentioned, is intermittent even while the excretion of sugar is uninterrupted. On the contrary, in any nutritive disturbance of the renal epithelium observed in diabetes, which has already been considered (p. 889), the causes of the albuminuria are to be found in its hypertrophic swelling and fatty infiltration. Now, since these changes border upon the physiological state, and form but the very first steps towards pathological changes, the appearance and disappearance of albumen from time to time is readily intelligible.

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[1] In amyloid degeneration, as in contracted kidney, the low specific gravity of the urine forms, as is well known, an important sign. This, of course, would be vitiated by the saccharinity in case of coincident diabetes mellitus.

There are still other facts which merit consideration in explaining this albuminuria, such as, in the first place, the circumstance that, according to Cl. Bernard's[1] statement, injury of the fourth ventricle at a point a little above the situation of the so-called sugar-point (Zuckerstich) gives rise to albuminuria. Since in many cases of diabetes an irritation of the floor of the fourth ventricle, analogous to the sugar-point, must be inferred, it is fair to suppose that, if the irritation become more widely diffused, albumen as well as sugar may enter the urine, and thus the albuminuria of diabetics arise. Moreover, we may suppose, at least in cases in which, as is so common, patients take a good many eggs with their animal diet, that the white of eggs eaten in great quantities occasions albuminuria, as has been ascertained by numerous investigators since attention was first called to it by Patrick Tégart, in 1845. Finally, too, the pyelitis which not infrequently occurs in diabetics (see p. 889), may give rise to albuminuria, but only in connection with the suppuration which is present. It has already been mentioned, however, that pus-corpuscles and other morphological elements—especially such as serve to indicate pyelitis, as epithelium from the pelvis of the kidney—are not, as a rule, found in the albuminous urine of diabetics.

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[1] Leçons, etc. p. 136.

Inosite was first detected in the urine of a diabetic by Vohl,[1] taking the place of the grape sugar, which gradually disappeared, so that the mellituria passed into an *inosituria*, the other phenomena persisting, particularly the increased urinary excretion. The amount of inosite was so considerable in this case that from 18 to 20 grammes could be extracted from the urine daily; afterwards inosite was found by Neukomm[2] also in a diabetic, and in this instance along with sugar; it was also found by Gallois[3] in five out of thirty-eight diabetics; and by Kuelz (Beitr. I. p. 119), in one case, together with sugar, too, in varying quantities, whilst in other cases he failed to find it when, as is more remarkable, the patients had eaten considerable amounts of inosite with their food (green beans). What significance attaches to the appearance of inosite in the urine is thus far wholly obscure. Besides diabetes mellitus, inosite occurs also in diabetes insipidus (q. v.), as well as in albuminuria (twice in twenty-five cases, according to Gallois), under quite unknown conditions. In one instance also Gallois saw inosite alternating with sugar in the urine of a rabbit which had been pithed after the manner of Bernard, whilst it was absent from the urine of other rabbits operated upon in the same way; just as, in general, it is often not found in human beings affected with diabetes.

Quite recently *acetone* and *alcohol* have been discovered in saccharine urine, accounting for its wine-like odor noticed by the older physicians—the former being altogether due to a decomposition of the *diacetate of ethyl* likewise present, and the latter, in part at least, to this cause, and in part proceeding perhaps from the sugar. Petters first discovered acetone in diabetic urine, and Kaulich confirmed this discovery in several cases, as did also Alsberg (see Ruickoldt), Burresi, Cantani, and others.

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[1] Archiv für physiol. Heilk. 1858. p. 410.

[2] Ueber das Vorkommen von Leucin, u. s. w. Inaug.-Diss. Zürich, 1859.

[3] Comptes rendus. 1863. I. p. 533, and De l'Inosurie. Paris, 1864.

C. Gerhardt ascertained that this urine containing acetone was colored red by chloride of iron, a reaction which Huenefeldt (F. Th. Schultze) had before noticed in a specimen of diabetic urine, and which led to the supposition that it contained diacetic acid, from which acetone is readily formed. Rupstein has recently confirmed this supposition by exhibiting the acid from diabetic urine. Rupstein also found alcohol in the same urine, and Kuelz (Beitr. II. p. 216) likewise found alcohol in the urine of a diabetic, and that, too, in a specimen fresh from the bladder. It appears from this, that in many cases the decomposition of the diacetic acid, and probably also the fermentation of the sugar, may begin while they are yet within the bladder. More commonly this does not occur until after the urine is voided, as we may conclude from the gradual disappearance of the reaction with chloride of iron and the increasing odor of acetone and alcohol.

Salisbury[1] professes to have found *cholesterine* in the urine in diabetes. I myself have seen a sediment of *oxalate of lime* at the very beginning of a case of diabetes, while yet the urine contained but a very small amount of sugar, in a woman forty-five years old, who was under observation for a considerable length of time.

By reason of the irritation exerted by the saccharine urine, and particularly the last drops stagnating and drying upon the mouth of the urethra and the surrounding parts, *a feeling of burning, itching, and inflammation* is easily brought about. In such cases the fungus, first discovered by Hannover in diabetic urine, is found on the external genitals also, under the prepuce, etc., as Friedreich has ascertained. In men balanitis, phymosis, and paraphymosis are thus produced ; in women, still more frequently, a distressing eczema or prurigo of the labia, which indeed not infrequently first calls attention to the diabetes.[2]

As regards the *function of micturition, incontinence* is observed in many cases, the nocturnal form, in particular, being of frequent occurrence in diabetic children, and on this account an examination of the urine should never be omitted in cases of nocturnal incontinence. The cause probably lies partly in the irritation which a highly saccharine urine exerts upon the walls of the bladder, and partly in the inability, due to the great accumulation of urine, to attend quickly enough to the desire to urinate, or in its not always being felt during sleep.

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[1] Amer. Jour. of the Med. Sci. XLV. 1863. p. 289.

[2] These affections are fully treated of by *G. de Beauvais*, De la balanite, etc., symptomatique du diabète. Paris, 1875.

Disturbance of the sexual function is not infrequently observed in men, the sexual impulse and the power of erection diminishing, and the testicles sometimes becoming atrophied, and even wholly disappearing (see p. 890). This decrease of sexual power, when it occurs, is, according to Seegen, one of the first symptoms of diabetes. As the disease improves under appropriate diet, the impotence also generally disappears, and we may often observe frequent alternations of reawakened sexual desire, and an increase of the diabetic symptoms. The impotence has been attributed to a too scanty secretion of semen, corresponding to the diminution of the other glandular secretions; but this is a conjecture for which there is thus far no foundation in facts.[1] For the rest, impotence is not by any means a symptom to be observed in all diabetics, and occasionally indeed an inordinately increased sexual power has been noticed, with frequent erections and pollutions. In women disturbances of the sexual apparatus are scarcely to be noted; menstruation goes on naturally, as a rule, and, as in any other illness, does not disappear until nutrition has suffered very materially. Even pregnancy has been seen to take place in diabetic women, according to Budge, Seegen, and others, but it seems to be frequently ended prematurely by abortion.

Behavior of the Digestive Apparatus.

The two most striking subjective phenomena, increased *thirst and hunger*, are scarcely ever wanting in a case of diabetes. Both of them, and more particularly the thirst, are in direct ratio to the excretion of sugar, rising and falling with it. Farinaceous and saccharine food, which make the urine richer in sugar, therefore usually very quickly increase the thirst also. The patient's *sense of taste* is commonly altered, being stale and clammy, and not infrequently, too, decidedly sweet—the latter being due probably in many instances to the presence of sugar, which, according to MacGregor, Nasse, Heller, and Lampferhoff,[1] is often found in the oral cavity. The transformation of the sugar into lactic acid is probably also the cause of the *oral fluid* in diabetics almost always showing an acid reaction—at all events, much more commonly than in a healthy person. Probably, too, the not infrequent occurrence of the thrush fungus in diabetics is due to the same fact (Friedreich).

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[1] *Tommasi* explains the impotence as due to the effect of the sugar in the blood upon the spermatozoa.

The *saliva* proper, especially the secretion of the parotid, when carefully collected without admixture of remains of food, mucus, and the like, has not generally been found to contain sugar (Bernard, Guenzler, Mosler, Harnack, and Kuelz), but in a few cases it seems to have contained sugar (Jordaô, Koch, and Pavy). Its reaction is sometimes found alkaline and sometimes neutral or feebly acid, whereas, as is well known, the normal parotid saliva is always alkaline after the first stagnant drops have flowed off. Kuelz (Beitr. II. p. 5) found the same differences also in the reaction of the saliva from the submaxillary glands.

The *tongue* seldom shows a normal state in well-marked cases of diabetes. According to Seegen, it is almost always increased in thickness, breadth, and volume, and commonly shows fine fissures and indentations, swelling of single papillæ or of whole groups of papillæ, and thickening of the epithelial layer, with islets of marked denudation. In milder cases, however, the tongue is commonly enough quite normal, or it is sometimes heavily coated, and at other times again strikingly glazed and red, so that in general its appearance varies widely, according to the state of digestion and the occurrence of improvement or aggravation of the general condition.

In advanced cases the *gums* are often softened and swollen, and bleed readily; subsequently, especially in somewhat elderly persons, they gradually shrink, the roots of the teeth become exposed, and the teeth so loosened as to fall out upon the slightest occasion. *Caries of the teeth* is quite common in diabetics, apparently in consequence of the habitual acidity of the oral fluid.

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[1] In *Karth*, De Dyscrasiâ Saccharinâ. Diss. Bonn, 1840.

The *appetite and digestion* often remain for a long time unimpaired, and, as has repeatedly been said before, even unusually hearty food, especially the saccharine and starchy, always seems able to appease the hunger for a short time only. But not infrequently, indeed, temporary disturbances of digestion take place, with signs of a gastric or intestinal catarrh, and such derangements are especially occasioned by a protracted, uniform, highly animal diet, thus impairing the effect of dietetic treatment.

Whether the *gastric juice* contains sugar has not yet been positively ascertained, but it is very likely that sugar may pass into it as well as into other secretions, especially as Cl. Bernard succeeded in detecting sugar in the stomach of animals after having injected it into the blood, and as Polli, MacGregor, Scharlau, Heller, and Frick found sugar in the gastric contents vomited by diabetics, even when hydrocarbons (*i. e.*, vegetables!) were excluded from the food. Griesinger's objection that this sugar may have been formed in the stomach by decomposition of the albuminates can scarcely be considered as warranted in the light of present views of the behavior of albuminous substances in the intestinal canal. In two cases Kuelz found sugar in the fluid obtained from the stomach with a syphon during fasting, both during and after the digestion of meat. Fonberg[1] had previously sought in vain for sugar in the vomited matter. Nothing is known in regard to other anomalies of the gastric juice. Bouchardat's statement in regard to a peculiar ferment in the gastric juice of diabetics is devoid of foundation.

Defecation shows no constant character, but, if there be no intestinal catarrh, a tendency to constipation is usually present, perhaps from the dryness of the fæces, which in turn depends upon the great losses of water through the kidneys.[1] Animal food, too, so long as it is well borne, favors constipation, because less of it remains undigested than of vegetable food. Sugar is found in the stools only when there is diarrhœa, and not always even then; in the ordinary solid motions of the diabetic it is not found at all, or only in doubtful traces (Heller, Beckmann in Gaethgens, Pettenkofer and Voit, and Kuelz). Not infrequently, as was noticed by the older physicians, the fæces are very deficient in biliary pigments, and even of a clay-like appearance. In the old accounts by MacGregor and Liman we find mention of the fæces containing urea, which must have been founded upon faulty methods of examination.

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[1] Ann. der Chem. und Pharm. LXIII. 3.

If we except the formation of sugar, morbid phenomena on the part of the *liver* are but seldom met with, although in corpulent patients, who are remarkably prone to diabetes (p. 867), we may discover an enlargement of the liver, due probably to fatty infiltration, and giving rise to no discomfort. Quite as little does the hyperæmia of the liver, so often found in the dead body, betray itself by specially noticeable clinical phenomena. Sometimes *jaundice* appears for a time, either as an accidental complication due to a catarrh of the duodenum, as I myself observed in one case, or as the result of compression of the bile-ducts by the overloaded blood-vessels or by the enlarged gland-cells (p. 885). In the case which I observed, no bile-pigment could be detected in the urine by means of Gmelin's test, perhaps because it was too dilute. It will be readily conceived that our knowledge of the state of the *biliary secretion* during life amounts to nothing. So, too, in regard to its condition in the artificial diabetes of animals, we find conflicting statements, Kuehte and Heidenhain[2] having seen it continue unchanged after the operation, whilst Naunyn observed it to become decreased in amount. (In regard to the post-mortem saccharinity of the bile, see above, p. 892.)

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[1] *Boecker* found 68.6 per cent. of water in the fæces of a diabetic, as the mean of six days' observation, the normal percentage being, according to *Berzelius* and *Wehsarg*, from 73 to 75.

[2] Studien des physiol. Instituts in Breslau. 1863. p. 69.

State of the Respiratory Apparatus.

The patient's *breath* commonly emits a peculiar, apple-like odor, similar to that of the urine (p. 907), and it is most probably due, like the latter, to acetone, and perhaps also to alcohol. But the great difficulty of an examination of the expired air has thus far precluded the recognition of this substance. (See Rupstein.)

Of the graver affections of the respiratory apparatus, *chronic pneumonia leading to phthisis* is almost the only one, as was stated under the head of pathological anatomy, although, were we to trust to the clinical phenomena alone, we should look upon it as less frequent than the autopsies indicate. Thus, in many cases, particularly in patients under favorable surroundings and good dietetic conditions, it is developed exceedingly slowly, and gives rise to very little trouble, so that it often remains wholly latent or only attracts attention at its very outset by the phenomena of a catarrh of the apex. In severe cases, on the other hand, it may pursue a very rapid course, and prove the cause of death when extensive lesions have taken place in the lungs. The attempt has been made to trace the development of the pulmonary phthisis of diabetes to the great loss of water, the drying of the tissues, and the resulting tendency to caseification, to destruction of inflammatory collections; but experience in diabetes insipidus—upon which, in spite of the heightened excretion of water, consumption does not supervene with a frequency in any wise striking (see "Diabetes Insipidus")—does not speak very much in favor of this view. Still less tenable is Fauconneau-Dufresne's theory, according to which the lungs become diseased in consequence of the great strain which they have to undergo in the combustion of the great quantities of sugar present in the blood. For, in the first place, the sugar is not oxidized at all, or only in the smallest amount; then, it is in just those mild cases in which the sugar formed from the meat diet, and often a portion, too, of that coming from the vegetables taken, is assimilated or "burnt," that the lung-affection more rarely occurs; and further, a heightened activity of the lungs has rather the power to prevent than to favor their becoming affected with chronic pneumonia and tuberculosis; whilst, finally, the notion that the lungs are roused to greater activity by the presence of sugar in the blood is wholly gratuitous and destitute of foundation in any known facts. We must therefore, it would seem, impute the tendency to pulmonary phthisis to the abnormal conditions of nutrition which are associated with the presence of unnaturally large amounts of sugar in the blood, and to the general marasmus.

The *symptoms* of the pulmonary phthisis of diabetics do not differ from those of the ordinary form of the disease. It need only be mentioned that sugar has been found in the bronchial mucus, and in the expectoration, as a whole, of such patients (Trousseau, Clinique Médicale; Kuehne, Lehrb. der physiol. Chemie. p. 24; compare also p. 892).

The *gangrene* of the lungs, which has occasionally been found post-mortem (p. 883), has this peculiarity: that, contrary to what happens in pulmonary gangrene under other circumstances, the sputum is entirely *odorless* (see Monneret, Arch. gén. 1839. VI. p. 300; Griesinger, l. c.; Charcot, Gaz. hebd. 1861, Août 23; Kussmaul, l. c., p. 9). Griesinger supposes that in the body of a diabetic, pervaded with sugar (and lactic acid), changes may go on of a different character from those which otherwise take place in disintegrating tissues, so that the ammoniacal compounds or volatile acids which, under other circumstances, give rise to the stench in pulmonary gangrene, are not developed or are very speedily changed. I consider it not unlikely that the volatile ethereal or alcoholic materials, such as acetone and alcohol, contained in the expired air, may, on the one hand, hinder the decay of the débris of gangrenous tissue, and, on the other hand, disguise the foul smell, thus acting as disinfectants and deodorizers.

State of the Nervous System and of the Organs of Special Sense.

In our previous discussion of the etiology and pathological anatomy of diabetes we referred to its association with affections of the nervous system and to their mutual causative relations, and we mentioned that it was not at all rare that a palpable lesion in the neighborhood of the medulla oblongata or of the sympathetic nerve-tracts was to be looked upon as the immediate cause of the disease; also that pronounced mental affections might precede diabetes or become developed during its course. But not only in these cases, but also in the numerous others in which no marked focus of disease is to be found in the nervous system, manifold nervous disturbances are present, which, however, do not always show a specially characteristic stamp, and which often enough betray themselves by such slightly expressed changes in the general health or in the several functions, that nothing but careful observation is capable of detecting them or of estimating them aright. Varying moods, irritability, a tendency to sadness and melancholy, a feeling of dullness and disinclination to bodily or mental exertion, are of common occurrence in diabetics, except possibly in the very mildest cases, and even in these cases we may ascertain by close questioning the presence of one or another of these symptoms, or that headaches or abnormal sensations in the limbs—a feeling of being asleep, formication, or even neuralgic pains, hyperæsthesia and partial anæsthesia are perceptible; that the sleep is disturbed, or that the memory is becoming impaired, and so on. According to Bouchardat, it would seem that weakness of the memory in particular occurs ten times as often in diabetics as in other persons of like age. *Motor* disturbances are less common than the sensory, with the exception of general *muscular weakness*, which is probably to be referred rather to defective nutrition of the muscular tissue itself by the saccharine blood than to changes in the nervous system. Muscular twitchings often occur, however, and even severe convulsions, especially in the lower limbs, whilst paralyses are scarcely ever present unless they depend upon some gross lesion of the central nervous system, such as an injury, a tumor, and the like.

The *decrease in the sexual desire* also depends upon a primary change of nervous organs, particularly upon an exhaustion or functional insufficiency of the nervous apparatus which presides over erection (compare also p. 909). Finally, vaso-motor and trophic disturbances not infrequently occur, which will be discussed further on. (See "Skin.")

A peculiar combination of nervous disorders, which has come to be designated as *diabetic coma*, occurs frequently towards the end of the disease, and for the most part somewhat suddenly. It seems that Prout first recognized this assemblage of symptoms, and even then noticed that forced marches and journeys, as well as fatiguing walks or excesses at table, particularly favored the occurrence of these peculiar phenomena. Since that time v. Dusch, Petters, Griesinger, Foster, Buerschaper,[1] Hilton Fagge,[2] Taylor,[3] and Kussmaul have made similar observations, and the latter especially has given a thorough account of these phenomena. Sometimes suddenly without any premonition, sometimes after a brief stage of agitation, with general uneasiness, oppression, anxiety, and pain in the region of the stomach, the patient becomes somnolent, tosses about restlessly, generally groaning loudly ; the pulse becomes excessively frequent, the arterial tension is low, the breathing is hastened and deep, although there is no impediment in either the upper or lower portions of the respiratory apparatus ; the extremities become cool, and even the general temperature of the body falls below the normal, and finally death ensues amid the deepest coma, sometimes after the supervention of twitchings.

The whole aspect presented by such patients, as well as, in particular, the exceedingly sudden and unexpected supervention of so deadly a catastrophe upon a condition previously tolerable, with no sign of immediate danger, makes it probable that we are dealing with a sort of poisoning, and that, too, by some substance arising within the body of the diabetic himself. The phenomena do not correspond to those of a uræmic intoxication, which many authors are inclined to assume, and indeed, with the unimpeded flow of urine, there is no occasion for its development. The appearance of acetone in the blood (see p. 891) may rather, as Petters would have us believe, be the cause of these peculiar phenomena, especially since, as Kussmaul has shown, very large doses of acetone given to animals give rise to symptoms of poisoning in many respects like these; but the effect of acetonæmia in man is not yet sufficiently well known to allow of a positive conclusion. Besides, the effect of alcohol is probably present also, it being developed from the diacetic acid at the same time with acetone (see p. 907), and perhaps that of still other unknown substances. Whether exertion and agitation, which in most cases precede the outbreak of these symptoms, favor a sudden accumulation or an increased formation of such substances, and, if so, in what manner, is thus far but a matter of conjecture.

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[1] Plötzliche Todesfälle von Diab. mell. Diss. Leipzig, 1870.

[2] Guy's Hosp. Reports. XX. 1873. p. 173.

[3] Ibidem, p 521.

Of the organs of special sense, the *eyes* are very frequently affected in diabetes. The most common form of disturbance of vision is occasioned by the *formation of cataract.* According to Roberts, it occurs once in 45, and, according to Bouchardat, once in 38 diabetics, whilst Griesinger, in a collection of 225 cases, found cataract mentioned in 20, and considers even this number as too small. It is for the most part in advanced cases that opacity of the lens occurs, especially those in which an abundant excretion of sugar is going on; but it also happens that attention is first directed to the diabetes by the disturbance of vision, and more especially by the very acute formation of cataract, completed in a few weeks—particularly if, as is exceptionally the case, the other symptoms are not very severe or annoying to the patient. As a rule, both eyes are attacked, as is usually the case with cataract from internal causes; but it is seldom that the opacity advances with equal rapidity in the two eyes, being behindhand in one (rather more commonly the left, as it seems), so that patients do not always become totally blind, for the reason that they do not live long enough for a perfect cataract to form in the second eye. The prospects from an operation for cataract are, in general, less favorable in diabetics than in others, although full statistics in regard to this point are wanting, since the results of cataract operations, in general, are much more favorable now than formerly.

The origin of cataract in diabetes was formerly attributed to the withdrawal of water, on the strength of Kunde's experiments,[1] who succeeded in producing an opacity of the lens in frogs by desiccation or by the introduction of substances having a strong affinity for water, such as common salt and sugar, under the skin—experiments which were afterwards repeated with the same result by Richardson[2] and Weir Mitchell.[3] On the other hand, A. v. Graefe, who first studied the pathology of diabetic cataract on the basis of an abundant experience, correctly pointed out that such lenses do not, like those of frogs, lose their opacity by being laid in water, and that they do not, like the latter, show any formation of vacuoles in their interior. Experience in diabetes insipidus, which does not specially predispose to cataract, also tells against its origin in mere deprivation of water. The abnormal constitution of the blood, its saccharinity, as well as that of all the tissue-juices, seems rather to influence the nutrition of the crystalline lens, and to favor the formation of cataract. This tallies with the observation that it is, for the most part (although, according to Griesinger, not invariably), seen in conjunction with an abundant excretion of sugar, and that, by improving the diabetic symptoms, we see it remain stationary, and increase upon the reappearance of sugar, of which Seegen has contributed two striking examples. For the rest, sugar has repeatedly been detected with certainty in diabetic lenses, as by Goldschmidt[4] of Breslau, O. Liebreich (H. Schmidt),[5] Fehling (R. Berlin),[6] and Stoeber.[7] The aqueous humor and the vitreous body have also occasionally been found to contain sugar (Carius-Knapp and Lohmeyer).[8]

Still other disturbances of vision occur in diabetes, although not so frequently as cataract; thus, according to v. Graefe, especially in the marasmic period, partial paralyses of accommodation, corresponding to the decrease of power in other groups of muscles. According to Haltenhoff,[1] we should include under this head many of the visual derangements which were formerly designated as *slight amblyopias* without objective signs (Lecorché),[2] especially as they may be improved by convex glasses, and, according to Pavy, by calabar bean also. In such cases the visual power commonly improves again with the improvement in the general condition and the increase of muscular strength. Furthermore, we observe *persistent and generally incurable amblyopia*, gradually passing into progressive atrophy of the optic nerve, a form which, according to v. Graefe, Lecorché, and others, apparently depends upon cerebral lesions which lead to trophic disturbance in the vicinity of the optic nerve. Finally, *hemorrhagic and inflammatory affections of the retina are observed*, resembling retinitis albuminurica (Jaeger, Desmarres, Galezowski, and Haltenhoff), and that, too, in some cases wholly unconnected with albumen in the urine.

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[1] Würzburger Verhandl. VII. 1856; and Arch f. Ophthalm. III. p. 275.

[2] Journal de la Physiologie. 1860.

[3] Amer. Jour. of the Med. Sciences. 1860. p. 108.

[4] Cited in *Ossowidzki.*

[5] v. Zehender's Monatsbl. XI. 1873. p. 492.

[6] See *Graefe* and *Saemisch*, Hdb. d. Augenheilk. V. p. 271.

[7] Compare *Knapp*, in v. Zehender's Monatsbl. 1863. I. p. 168.

[8] Ztschr. f. rat. Med. N. F. 1854. V.

Impairment of the hearing, without recognizable cause, has likewise been noticed, but, on the whole, rarely (in one case by Jordaô, in three by Griesinger, and in one by Kuelz, Beitr. I. 1). Far more frequently a nervous *roaring in the ears* occurs, depending apparently upon anæmia and debility, and disappears again with the improvement of the strength. Together with impaired hearing, Jordaô found in his case a *blunting of the senses of smell* and *taste* (for pepper). We have already mentioned other derangements of the taste due to digestive disturbances, or an abnormal condition of the fluids of the mouth (see p. 910).

In conclusion, as regards the secretions appertaining to the organs of special sense, it should be mentioned that sugar has been found in the *tears* by Fletcher and Gibb, but not, on the other hand, by Kuelz (Beitr. II. p. 134), even when the patients had eaten freely of the hydrocarbons. Lampferhoff[3] and Fletcher state also that they have found sugar in the cerumen of the ears.

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[1] v. Zehender's Monatsbl. f. Augenheilk. Oct. 1873. p. 291.

[2] Gaz. hebdom. 1861. p. 717. Sur l'amblyopie diabétique.

[3] *Karth*, loc. cit.

State of the External Integuments.

Dryness of the skin is a very common phenomenon in diabetics, but it becomes excessive only when the excretion of urine and sugar is very great. Then the skin becomes rough, harsh, and scurfy, and shows fine, branny desquamation in its larger folds. So soon as pulmonary phthisis is added and has advanced moderately, *hectic sweats* are usually not wanting, notwithstanding the existence of copious urination, although they are perhaps not so profuse as in other consumptives. Nor is it so very rare for diabetics to show copious general or local sweating, especially upon moderate muscular exertions, such as would not have made them sweat when in health. In rare instances also *excessive unilateral sweating* has been observed—once by Koch[1] and Nitzelnadel,[2] upon the left half of the face, in a man thirty years old; twice by Kuelz, in a man fifty-one and another forty-six years old, upon the left and right halves of the face respectively, in connection, apparently, with changes of the sympathetic on the affected side.

That *sugar* may be present in the *perspiration* was known to the older physicians (Autenrieth and others), and Willis noticed that the branny scales from the skin of the legs had a decidedly sweet taste. Perhaps, however, the remains of dried urine may have given rise to the taste in those cases. But the sugar is not found in all patients, or at all times in one and the same patient. MacGregor, Lehmann,[3] Hoefle,[4] Stockvis,[5] Ranke,[6] and Kuelz (Beitr. II. p. 135) sought for it in vain, the latter in as many as ten cases. On the other hand, Nasse, Heller, Lampferhoff, Landerer,[7] Fletcher, Semmola,[8] Griesinger, Bergeron and Lemaitre,[9] and Koch found it, and sometimes, indeed, in very notable quantities. Fletcher, for instance, extracted six and a half grains of sugar from a piece of flannel three inches square, which had lain on the skin for forty-eight hours; Foster found six grains to the ounce in one case (XIII.); and Semmola about two per cent.; and the latter, as well as Griesinger in particular, observed that the sugar was wanting or considerably decreased in the urine so long as it was being excreted in the sweat—a circumstance which, as Griesinger rightly points out, may easily cause a deceptive appearance of improvement.

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[1] Ueber D. mell. Diss. Jena, 1867.

[2] Ueber nervöse Hyperidrosis und Anidrosis. Diss. Jena, 1867.

[3] Lehrb. der physiol. Chemie. II. p. 336.

[4] Chem. und Mikrosk. am Krankenbette. p. 306.

[5] See *Vogel.* p. 484.

[6] *Pavy*, p. 104. (of German edit.) Anm. von *Langenbeck.*

[7] See Canstatt's Jahresb. 1846. II. p. 52.

[8] Comptes rendus. 1855. Sept. p. 430.

[9] Arch. gén. de méd. IV. 1864. p 173.

Driessen[1] tells of a soldier, thirty-three years old, whose copious perspiration smelt of *sour apples*, and made his linen quite stiff, and did not subside until the signs of specific diabetes had plainly appeared.

Itching of the skin, as has already been stated (p. 908), is very commonly met with on the genitals, being then generally due to the dried urinary sugar; but sometimes, too, it is felt in the whole skin or over large areas, without any discoverable anatomical change, so that it is probably a purely nervous phenomenon, occasioned by the irritating effect of the saccharine blood upon the sensitive terminations of the nerves, or by central disturbances. The abrasions occasioned by scratching, as well as other slight injuries of the skin, blistered surfaces, and the like, often heal with surprising difficulty, spread in a malignant manner, and become gangrenous.

As a general thing, there is a great tendency in diabetic patients to inflammations and the formation of abscesses in the skin, more especially to *furuncles* and *carbuncles*. The former, in particular, may appear in great number at a time, while yet the other phenomena are not very well marked, and may first call attention to the diabetes. Carbuncles, on the other hand, do not appear, as a rule, until the later period of the disease, and they are then not infrequently the immediate cause of death. Occasionally, to be sure, carbuncles also appear in persons in whom previously no signs of diabetes have been recognized, but in whom the disease is first discovered during the progress of the carbuncular affection. A. Wagner has collected a few such cases from the observations of himself and others.

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[1] Diss. de phosphoruriâ et d. mell. Groning. 1818. See in *Griesinger*.

But other forms also of *gangrene of the skin* and *gangrene of individual members*, the toes or even a whole limb, are of not infrequent occurrence. Marchal de Calvi particularly called attention to this occurrence of gangrene in diabetics, which had already been noted, but not carefully observed, by the earlier observers, such as Carmichael,[1] Champouillon,[2] Landouzy,[3] and Billiard;[4] and numerous observers have established its frequency. The symptoms and course of this gangrene are very like those of senile gangrene, and this perhaps has led to the supposition that, in the one case as in the other, an obstruction, inflammation, and degeneration of the arteries lay at its foundation. Now, although an "obliteration" of the arteries concerned has been found in many of the cases of gangrene in diabetics examined after death, yet the proof is not thereby furnished that this was the cause of the gangrene; and, in particular, embolic and atheromatous processes, which are the usual causes of senile gangrene, have not been found, except in persons of advanced years. According to Dickinson, degenerations of the arteries would seem, indeed, to be remarkably rare in diabetes, and he therefore seeks for the cause of the gangrene in a deficient nutrition of the tissues by the altered blood, or in an abnormal coagulability of the latter.

Falling-out of the nails, without any appearances of inflammation, was seen by Folet[5] in a diabetic woman.

Lastly, *œdema* takes place, especially of the lower limbs, mostly as the result of advanced cachexia, and only exceptionally of a complicating severe affection of the kidneys. (See above, p. 905.)

General Phenomena.

The *general health* remains for a long time undisturbed in the slighter cases of diabetes—those which develop slowly, and in which sugar appears in the urine, in general, only after eating vegetables, and again disappears, wholly or for the greater part, after refraining from them. A proneness to fatigue, however, and a decrease of bodily, and often of mental power, generally set in very early, but they are commonly so slight that they are only noted and observed by very careful persons. Since many of these patients are well favored and even remarkably corpulent (see p. 867), their outward appearance in no wise reveals anything morbid, and it is only when they lead an injudicious mode of life that their appearance depreciates rapidly, as the excretion of sugar, the thirst, and the other symptoms get the upper hand. The disease behaves differently in the severer cases, pursuing a more rapid course, with the typical phenomena in the highest perfection. Patients of this sort often become emaciated in an astonishingly short space of time, to such an extent as happens only perhaps with cancers of the internal organs; they grow old prematurely, have a cool and dry (and in the very advanced stages also a bluish-red) skin, and usually a depressed and anxious expression of the countenance, which derives something peculiar also from the smacking and choking movements of the mouth and tongue, which are constantly dry. To such patients, indeed, we may apply the somewhat exaggerated expressions of experienced physicians, "that the mere look of a diabetic is often abundantly sufficient to reveal the nature of the disease, without the necessity of putting a single question." (See Pavy.)

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[1] Med. Times. X. 1846. p. 110.

[2] Gaz. des hôpitaux. 1852. p. 190.

[3] and [4] Ibid. No. 51 and p. 212.

[5] Gaz. hebdom. de méd., etc. 1874. No. 5.

Fever, in the absence of inflammatory complications, does not occur in diabetes; on the contrary, the temperature is very commonly, as was found by Bouchardat[1] and many others after him, somewhat below the normal—between 95.9° and 97.7° F.; and even temperatures as low as 93.2° F. have been observed in the axilla (J. Vogel and Dickinson). It is generally patients very far advanced in the disease and highly emaciated who show such a low temperature. It is caused by just those particular circumstances which are found in severe cases associated with highly impaired nutrition: in the first place, chiefly by the disappearance of the subcutaneous fat, thus highly promoting the escape of heat; and, in the next place, by the ingestion of large quantities of cold drink to allay thirst. The influence of the latter was particularly ascertained by Foster (Clin. Med. p. 264), in an experiment in which he measured the temperature of a diabetic whom he had take his drink cold at one time and warm at the next, the conditions otherwise being the same as far as possible. The following table shows the results:

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[1] Mém. de l'acad. de méd. 1852. XVI. p. 157.

	Mean daily temperature.	Quantity of urine in 24 hours.	Remarks.
I.	97.3° F.	100 ounces.	Cold drink only.
II.	97.1	92 "	
III.	97.7	112 "	Warm drink only.
IV.	98.4	100 "	
V.	98.3	112 "	
VI.	98.3	112 "	
VII.	97.9	96 "	
VIII.	98.4	100 "	
IX.	98.2	100 "	Cold drink only.
X.	97.2	96 "	

Finally, too, the loss of sugar and the abatement of heat thus resulting may exert some influence upon the lowering of the temperature, although it has no such great effect as was formerly supposed, and is now by many, who consider the loss of "heat material" as the only cause of the abnormally low temperature of the diabetic. The amount of heat lost in twenty-four hours, in consequence of the non-oxidation of sugar, even were several hundred grammes of the latter excreted daily, is of no importance to an adult man, for the increase of temperature which the body would gain at any given moment by its gradual combustion is so slight that it would have no noticeable effect upon the normal variations, or would be counterbalanced by other occurrences. By wholly depriving a man of food for a day we should scarcely succeed in lowering his temperature as much as, it is asserted, is effected by the loss of a couple of hundred grammes of sugar. Now, it is particularly in diabetes, and above all in the very highly developed and severe cases which show the lowering of the temperature, that an unnaturally large amount of other sorts of nourishment is taken—more than enough to cover the escape of sugar and heat (pp. 898 and 908). But, finally, as

Griesinger has rightly pointed out, there is no constant relation at all between the bodily temperature and the excretion of sugar, as would have to be the case if the lowering of the temperature were governed by the loss of sugar. We see in one and the same patient, and in different patients, a normal or a lower temperature with the most varying degrees of saccharinity of the urine. But, if the objection be made that, in those cases in which a lower temperature is found with a trifling excretion of sugar in the urine, the sugar may be excreted by other channels than the kidneys, then the cases in which the temperature is not lowered, notwithstanding a copious secretion of sugar by the kidneys, are all the more conclusive.

The disappearance of sugar from the urine during intercurrent febrile affections (p. 874) has been thought to admit of explanation by an augmentation of all combustive processes occurring with the fever, and accordingly the heightened temperature of the diabetic has been referred to the combustion of the sugar which would otherwise have escaped unoxidized. The notion that fever consists of a simple increase of the normal processes of metamorphosis of elements has, however, been shown to be untenable, and it has thus been made clear that the combustion of a few hundred grammes of sugar in twenty-four hours can accomplish no considerable and persistent elevation of temperature. The reason for the disappearance of the sugar during febrile affections may perhaps be sought for chiefly in the diminution of the food, and very likely also in more profound alterations of the metamorphosis with which the febrile condition is associated. The excretion of sugar is not arrested by all febrile affections, and one and the same febrile disease does not exert the same effect in every case, instances of which have been given elsewhere (p. 875). It was there pointed out also that probably different cases of diabetes—the milder and the severer—behave differently in this respect. If, then, a patient who excretes sugar only upon eating freely of hydrocarbons—*i. e.*, when on vegetable diet, and even then not so much as corresponds to the whole amount ingested—be attacked with a febrile affection, during which he takes and digests considerably less of the hydrocarbons, he will naturally excrete little or no sugar. On the other hand, a diabetic who passes sugar, even upon a pure meat diet, will continue, even during the fever, to excrete the small quantity of hydrocarbons which he takes wholly or in great part in the form of sugar.

Mention has before been made of some other changes of the urine and of the several constituents of the urine in fever (pp. 901 *et seq.*).

With the aid of the great Munich respiration apparatus, Pettenkofer and Voit have undertaken experiments upon the total nutritive changes (Stoffhaushalt) which take place in a diabetic person, the results of which are shown in the following table. The patient upon whom the experiments were made was a peasant twenty-one years old, weighing from fifty to fifty-five kilogrammes, who had been ill for several years with increasing debility, hunger, opacity of the crystalline lenses, etc., and who at the time of the investigation, as it appears from his own statement, was in an advanced or severe stage of the disease.

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	Hunger (diet of water, salt, and meat extract).	Very abundant mixed diet.	Medium diet.	Food destitute of albumen.	Food rich in albumen.	Mixed diet.	Mixed diet in two half-days.
Carbon expired.	502	795	621	618	629	659	660
By day	. .	. .	. .	. .	. .	359	345
By night.	. .	. .	. .	. .	. .	300	315
Watery vapor given off. . . .	721	759	764	762	658	612	649
By day.	. .	. .	. .	. .	. .	309	358
By night.	. .	. .	. .	. .	. .	303	291
Oxygen taken up.	344	792	680	610	613	572	578
By day.	. .	. .	. .	. .	. .	278	282
By night.	. .	. .	. .	. .	. .	294	296
Quotient $CO_2 : O$.	106	73	66	73	74	83	83
By day	. .	. .	. .	. .	. .	90	89
By night.	. .	. .	. .	. .	. .	75	77
Urea.	28.5	100.7	48.0	19.4	62.4	49.8	65.9
By day	. .	. .	. .	. .	. .	29.7	35.4
By night.	. .	. .	. .	. .	. .	20.1	30.5
Sugar.	52	644	464	429	149	394	535
By day	. .	. .	. .	. .	. .	246	275
By night.	. .	. .	. .	. .	. .	148	260

Comparing this with the ingesta and excreta of healthy adults, and particularly with such as the same investigators found, under circumstances as like as possible, in non-diabetics, we find: 1. *Urea* is generally excreted in larger amount than in healthy persons on a similar diet, but by no means without exception as regards the individual days of the experiment. Particularly upon a diet free from albumen, the daily excretion of urea of the diabetic (19.4) was considerably less than that of the person compared with him (27.7), and, what is specially remarkable, very much—nearly 32 per cent.—less than while fasting (28.5), whilst the person compared excreted as much, or but little less, under the former condition as under the latter. If we might draw any conclusion from this one experiment, it could be only this, that in the diabetic a non-azotized diet effects more saving of albumen than in the healthy. A single experiment, however, for one day, when the effects of a different diet taken during the time immediately preceding must still be in action, does not warrant any such conclusion; and other experience in diabetes does not favor the idea that by excluding albumen from the food a greater proportion of the nitrogenized matter of the body can be saved than in a healthy person. The reasons for the increased excretion of urea have been given elsewhere (p. 898), together also with the experience of others in regard to it. It is there stated, also, that Pettenkofer and Voit, by an immoderate supply of nitrogen, outstripped its excretion in the urine and fæces, and were therefore able to effect an accumulation of azotized material in the diabetic person. 2. In all the experiments less *carbonic acid* and *watery vapor* was excreted, and less oxygen taken up from the air, than by the person compared. 3. The *ashy elements* in the urine were proportionate to the increase of urea, and, like the latter, generally exceeded the ingestion by a slight amount. (See above, pp. 903 and 904.)

Similar results were obtained somewhat earlier by Gaethgens, by comparing for a longer time his own sensible excreta with those of a diabetic living under nearly the same dietetic conditions. He found that in the latter a larger amount of urea, sulphuric and phosphoric acids, and chloride of sodium was excreted than in health; that more water passed off by the urine and fæces than was contained in the ingesta, probably in consequence of the body parting with it in increased amount; and that only an abnormally small amount of water remained to be disposed of by perspiration. Moreover, an estimate of that portion of the carbon which did not reappear in the sensible excreta indicated that the carbonic acid must also have undergone decrease as well as the inspired oxygen. The heightened excretion of solid constituents, especially urea, was to be explained, upon grounds already adduced (see p. 898), by an increased decomposition of albumen. Under the use of bicarbonate of soda (7.81 grammes a day), as well as that of benzoate of soda (8.05 grammes a day), the interchange of matter took essentially the same course, except that the sensible excretion of water was not only not covered by the ingestion with the food of water as such, but also not even by, in addition, that estimated to have resulted from the oxidation of hydrogen and from the loss of bodily weight. Thus there was no water at all left for the perspiration, but, on the contrary, still more water must have been absorbed insensibly, and that, too, in quantities not in accord with our ideas of the hygroscopic properties of the external integuments and of their capacity to take up water from surrounding media. We cannot avoid suspecting, therefore, that, in spite of every precaution, there was some source of error on the part of the patient, as is so liable to happen in experiments upon diabetics.

A few observations have been made by others also upon the state of one or another product of metamorphosis, and they are in perfect accord with the results already adduced. Thus, a decrease of the *carbonic acid* expired was asserted by Genzke, and afterwards ascertained in a more exact manner by C. Schmidt,[1] Boecker, and Bartels. A decrease of the carbonic acid and watery vapor together, *i. e.*, of the so-called *insensible transpiration*, has been estimated by numerous investigators—by Vogt, Nasse, Boecker, Reich, Mosler, Buerger, and Engelmann-Kuelz[2]—by a comparison of the so-called sensible ingesta and excreta with regard to the weight of the body, after the method of Sanctorius. It cannot be immediately concluded from that, as many, indeed, have done, that the watery transpiration is necessarily diminished, since it may be that the carbonic acid alone takes part in the decrease, the escape of water remaining unchanged. This, however, is not probable, for, in the first place, so much water escapes with the sensible excreta, particularly the urine, that there is little left for transpiration; in the second place, if the decrease of carbonic acid alone lowers the insensible excreta, it must be diminished to a quite extraordinary degree, which the condition of the patient's health in other respects scarcely warrants us in thinking; and finally, a diminution of the cutaneous transpiration, consisting chiefly of watery vapor, is indicated by the dryness of the skin and the lack of perspiration which is so common. But it must not by any means be considered as a rule without exceptions, that the insensible excreta of every diabetic are at all times reduced below the normal amount. It is more likely that they vary very much, as Kuelz observed in a case, and in particular the insensible loss of weight may rise to the normal level again in connection with improvement of the other phenomena.

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[1] Charakteristik der epid. Cholera. Leipzig und Mitau. 1850. p. 160.

[2] Beitr. II. p. 32.

In regard to the *total* elimination of water, *i. e.*, the sum of that given off by the skin, lungs, kidneys, and intestine, little is known. It seems to follow from Gaethgens' investigation, that it may be greater than corresponds even to an ingestion sufficient to quench the thirst—at all events, greater than in healthy persons on the same sort of diet. In such a case, then, more water would enter the urine than would correspond to the reduction of the water of perspiration, and would have to be furnished from the water and hydrogen of the body (see above, p. 894). In other cases, however, the total excretion of water may correspond to the ingestion of water and hydrogen, or be smaller still, only the distribution of the water being changed, so that an abnormally greater portion of it goes to the sensible excreta (the urine) than to the insensible.

But we must bear in mind that it is not the *absolute* amount of the one or the other excretory product, by which, apart from the loss of sugar, the metamorphosis in a diabetic is distinguished from that of a healthy person, but the *relative* amount as compared with that ingested. A diabetic may excrete, even at the height of the disease, quite normal amounts of urea, carbonic acid, water, and salts, without suffering any loss of bodily material; but the quantities are abnormal with regard to the food taken, upon which a healthy person would either excrete more or gain in weight. The difference is due to the excretion of sugar. If, therefore, it be possible for a diabetic to prevent the excretion of sugar by *selected* diet, his metamorphosis will probably not differ at all from that of a healthy person. Nevertheless, he remains a diabetic so long as he cannot assimilate hydrocarbons like a healthy person. On the other hand, a diabetic who should excrete sugar even when on an exclusive and really pure albuminous diet, would behave abnormally under all circumstances—which has not yet been observed.

Finally, be it remembered that, as I have stated above (p. 899), a *specific* destruction of albumen seems to occur independently of the augmented ingestion of nitrogen and of the heightened secretion of urine.

Theory of Diabetes.

A theory of diabetes, in order to be satisfactory, should (1) explain the appearance of sugar in the urine, and that, too, in quantities readily recognized; and (2) establish the connection between the mellituria and the most important remaining symptoms of the disease.

The numerous theories which have been upheld in recent times in regard to the appearance of sugar in the urine are all closely connected with investigations, in which Cl. Bernard led the way, concerning the formation and excretion of sugar in the system. Bernard found the blood of the hepatic vein to be rich in sugar, whilst the blood of the portal vein contained no sugar whatever, or but mere traces of it; furthermore, he discovered sugar in the livers of animals fed entirely on meat; and from these facts, which were speedily confirmed by other investigators, such as C. G. Lehmann, C. Schmidt, and Frerichs, he concluded that sugar was formed in the liver under normal conditions. He afterwards discovered, as did Hensen at the same time, that the liver contained a substance closely resembling sugar in the arrangement of its elements, and very readily changed into sugar, especially under the influence of an animal ferment—*glycogen*, in which he now perceived the first step in the formation of sugar in the liver. The transformation of the one into the other seemed to be constantly effected by a *ferment of the liver*, specially demonstrated by Bernard, and the sugar thus formed and carried into the circulation was consumed, or, according to the older notion, burnt up in the lungs. Finally, the famous experiment of cervical puncture pre-eminently favored the idea that this whole process of sugar-formation in the liver was governed by the *nervous system.*

In accordance with these expositions, variations in the amount of sugar formed in the liver, and carried from thence into the blood, were referable to various causes. The amount of sugar contained in the blood might vary according to the abundance of glycogen or ferment in the liver, and according as the function of this gland was carried on sluggishly or briskly by reason of the variable quantity of blood contained in it.

Bernard found the *amount of glycogen* contained in the liver to depend upon the quantity, and especially upon the quality of the food taken. In regard to the *amount of blood* contained in it, the nerve-trunks proceeding from the medulla oblongata were undoubtedly capable of exerting an influence; concerning the variable *amount of ferment*, Bernard himself did not undertake any researches, but experimental data upon this point were soon contributed by others.

Finally, variations in the *consumption* of the sugar formed, in normal or abnormal quantity, were referable to manifold causes. Any increase in the saccharinity of the blood, from any of the causes mentioned, may or must give rise to mellituria, since—and this, too, was made out by Bernard—as soon as the amount of sugar in the blood exceeds a certain limit, from 0.25 to 0.3 per cent. in dogs, it passes over into the urine.

This is, in outline, the doctrine of sugar-formation and of diabetes mellitus, such as Cl. Bernard gradually elaborated it in the course of his investigations and his unprecedentedly brilliant discoveries, and such as still serves as the point of departure for all the theories since broached. But the foundation of this doctrine, the glycogenic function of the liver, was at once combated, and in the first place by Pavy, who explained the formation of sugar as a *post-mortem process.* Pavy found sugar in the blood of *all* parts of the vascular system, including the hepatic vein and the right side of the heart, in about equal but very slight amount, even in the tissue of the liver itself, if immediately removed from the living animal and examined without loss of time; but, on the contrary, in the dead liver he found an amount of sugar constantly increasing up to a certain limit from the beginning of death. He satisfied himself, moreover, that various circumstances—such as struggling on the part of the animal employed in the experiment, violent muscular movements, pressure upon the abdomen, and the like—were capable of increasing the saccharinity of the blood even during life, and he ascribed Bernard's varying results to disturbances and sources of error of this sort. According to his view the hydrocarbons taken with the food, and perhaps also certain products of the decomposition of albumen, are normally stored up in the liver in the form of glycogen, and this is not changed into sugar but into fat, which serves for the formation of bile. Under abnormal conditions the glycogen becomes converted into sugar, and thus diabetes is developed. Pavy's statements were corroborated and extended by numerous investigators, such as Marcet,[1] MacDonnell, Schiff, Tscherinoff, Meissner and Ritter, and Eulenburg, and thence arose a controversy which is not yet over, chiefly in regard to the detection of sugar in the normal and still living liver and in the blood. It is certain, from the points expressly made by Pavy, that Bernard, at least in his earlier contributions, overrated the formation of sugar in the liver; but it is not thereby proved by any means that it does not take place in general, and, indeed, this is not maintained by Pavy—who always found traces of sugar in the liver—but by his followers.

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[1] In *Pavy*, Med. Times and Gaz 1865. p. 380.

That the *blood* contains sugar was demonstrated by many of the older observers after Thomson,[1] and this has been repeatedly verified, in renewed and carefully conducted observations, by Kuehne, Tieffenbach, Lusk, Harley,[2] and Bock and Hoffmann; in man particularly, sugar is admitted by C. Schmidt, Figuier, and Bock and Hoffmann to be a normal constituent of the blood.[3] It is found in the most diverse vascular districts, not only on the way from the liver to the heart, but also in easily accessible arteries and veins, the opening of which can scarcely be considered as a perturbative procedure favoring the formation of sugar; furthermore, it has been found in the capillary blood removed by cupping, and finally, too, in animals that had not eaten either sugar or starch. *It cannot be doubted, then, that sugar is formed in the healthy organism, and that it is constantly present in the blood. But the question of the glycogenic function of the liver is likewise decided at the same time and in the affirmative.* In accordance with our present knowledge, we must regard the liver alone as the original source of the sugar in the system—apart from the conversion of starch into sugar which takes place in the digestive canal, as well as the formation of sugar of milk in the secreting breast, which does not now come under consideration. This is shown, in the first place, by the fact that, if the liver be extirpated or isolated from the circulation, or made incapable of performing its functions by any other means, such as ligation of its vessels *en masse*, poisoning with arsenic, etc., the sugar at once disappears from the blood; and, in the next place, by the behavior of the *glycogen* in the system,—that body which stands in such close connection with the formation of sugar, and which is undoubtedly to be considered as its prototype. Everything, then, which interferes with the formation of glycogen tends also to prevent the formation of sugar.

Glycogen occurs regularly and in noteworthy amount only in the liver and the muscles.[1] In the latter, however, it is contained in far smaller quantity, in proportion, than in the liver; it disappears from them during fasting, or under certain sorts of diet, much more speedily than from the latter, and, *vice versâ*, appears in them more tardily under proper feeding ; and, finally, it is not found in them at all under conditions in which glycogen is formed in the liver, such as feeding with gelatine or the hypodermic injection of glycerine (Luchsinger, [b], pp. 16–42). We may therefore conclude with certainty that the liver is the chief, if not the only organ which forms glycogen by the transformation of matter introduced from without, and that the muscles possess this power to but very slight extent, or not at all, but derive their glycogen from the liver, either directly or in the form of sugar. Both substances, glycogen and sugar, are consumed by them in their contraction, and any casual superfluity is probably stored up as glycogen, which seems to be transformed into sugar again only with the activity of the muscle.

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[1] Philosophical Magazine. 1845. XXVI. according to *Bock* and *Hoffmann* (c), p. 2.

[2] According to *Dickinson* (b), p. 7.

[3] *Abeles* has also recently corroborated the normal presence of sugar in the blood (Wiener med. Jahrb. 1875. p. 269).

The diet, as Bernard had found, exerts the greatest influence upon the *quantity of glycogen* in the liver. Our knowledge upon this point has been essentially enriched by numerous investigations during the past few years, which have given the following results :[2] a decrease of the hepatic glycogen, even to entire disappearance, occurs as the result of *fasting*, and with variable rapidity, according to the stock of glycogen on hand, which, in turn, is dependent upon the previous dietary. In rabbits, from four to eight days of fasting transpire before the glycogen wholly disappears from the liver, and in dogs as many as from fourteen to twenty-one, and probably, according to Poggiale's researches upon the contained sugar, still more. Feeding with *hydrocarbons* produces the greatest increase in the amount of glycogen, and it is to be noticed after a few hours of digestion ; and, in particular, *grape-sugar*, *cane-sugar*, *levu-*

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[1] This is true, as is well known, only of the extra-uterine period, which alone interests us at present. During fœtal life glycogen is found in the most various localities, likewise during diseases—for instance, according to Kuehne, in the lungs in pneumonia.

[2] Compare the works on glycogen mentioned in the bibliography, and especially the very recent work (b) by *Luchsinger*.

lose, and *inuline*, besides *sugar of milk* and *galactose*, and finally and quite especially, *glycerine*, are characterized as great producers of glycogen.[1] *Mannite* and *gum* have no effect upon the amount of glycogen. *Fat* seems to cause only a very slight increase of the hepatic glycogen, which may, indeed, be referable to the setting free of glycerine in the intestinal canal by separation and saponification, since feeding with *fatty acids*, as well as with *lactic acid*, gives a negative result, according to Luchsinger and Salomon. According to Bernard, Salomon, and Luchsinger, in opposition to M'Donnell, *gelatine* is to be considered as a feeble producer of glycogen, whilst the effect of *albumen* is doubtful. Bernard, indeed, found an abundance of glycogen (or sugar) in the liver in dogs fed on meat, and Naunyn in hens which had for a long time been fed upon thoroughly boiled meat; but, since the muscles contain glycogen, fat (glycerine), and gelatine, *i. e.*, glycogen-producers, Bernard's experiments are not conclusive, and others, which were made with pure albuminous substances, are opposed to Naunyn's. Pavy and Dock found *no* increase of glycogen on feeding with white of egg, and Tscherinoff, Weiss, and Luchsinger (in opposition to Bernard), none on feeding with fibrine.

Many have sought to explain the process which follows the development of glycogen from the so-called glycogen-producers—that is to say, the sugars and glycerine—as a diminution or hindering of the conversion of albumen. It would seem, according to this theory, that the glycogen and fat, which latter arises from the destruction of albumen which is continually taking place in the body, are stored up, and not further oxidized, provided more readily oxidizable materials, such as plain sugar or glycerine, be ingested and take possession of the oxygen. This view may now be regarded as disproved, and for this reason, to say nothing of others (see Luchsinger), that other substances, oxidizable with equal readiness, such as lactic acid, vinous acid, fat, and fatty acids, do not have this effect. We must rather assume that there is a direct conversion of these substances into glycogen, by appropriation of water, division, synthesis, or other complex chemical changes.

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[1] Experiments in feeding with starch give no indubitable result, because, according to *Bruecke*, starch is changed during digestion into erythrodextrine, which agrees with glycogen in most of its reactions.

All these processes of the conversion into glycogen of materials taken in from without, are, for reasons which have already been stated, to be referred especially or exclusively to the liver. It is therefore not a matter of indifference in what locality the glycogen-producers become incorporated with the body. They furnish the greatest quantity of glycogen when they are introduced into the stomach, or into a branch of the portal vein, or into the vein itself; much less, on the contrary, and, if in small amount, even none whatever, if injected under the skin or directly into the blood, the portal vein being tied; for in the latter case they are diffused through the whole circulation, only a fractional portion reaching the liver, and, besides, they are excreted from the blood unchanged, at least in part.[1]

The power of the liver to form glycogen is associated with the normal function of the hepatic cells. We might well suppose *à priori* that this power is derived solely from the peculiar conditions of the hepatic circulation, particularly from the retardation which the stream of blood undergoes in the portal system, and which must be so highly favorable to the interchange of matter between the blood and the tissues. This idea is opposed, however, by weighty facts, above all by the fact that, according to Saikowsky and Luchsinger, the formation of glycogen ceases when the hepatic cells are rendered incapable of performing their functions by poisoning with arsenic, phosphorus, and the like, but not, according to Luchsinger, after procedures which give rise to an acceleration of the portal circulation, such as the cervical puncture or poisoning with curare.

Schiff's observation, too, that in frogs the formation of sugar (probably by a transformation of glycogen) continues for even a *longer* time (sixteen days) after ligation of the portal vein, must tell against this theory and in favor of the specific glycogen-forming action of the hepatic cells.[2]

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[1] As regards sugar, these statements have been current since the time of *Bernard*, and have been many times confirmed; as regards glycerine, *Luchsinger* has furnished the proof.

[2] As regards the formation of sugar, experiments made by Oré, Moos, and Pavy with

As glycogen is formed likewise from sugar injected under the skin, although, for the reasons above adduced, in relatively smaller quantity, it follows that no special preparation of the sugar in the stomach or intestine is necessary (Luchsinger).[1]

If the liver forms *glycogen* in its cells, and if *sugar* is constantly proceeding from it, no matter whether the amount be large or small, there is nothing more obvious than the supposition that the glycogen is continually being changed into *sugar* on its way from the cells into the blood of the hepatic vein. For this a *ferment* is necessary. Bernard produced such a sugar-forming ferment from the liver, and, according to his assumption, it would seem to be contained only in a certain number of the hepatic cells, glycogen being found in the others, and the action of the two upon each other being ruled by nervous influence. Hensen and von Wittich also express themselves as considering the seat of the ferment to be in the hepatic cells, while the majority of other investigators place it in the blood, because glycogen treated with blood outside the body is changed into sugar, and, if introduced into the circulation of the living body, increases the saccharinity of the blood, and even makes the urine saccharine. Experiments of this sort have been particularly undertaken by Pavy, whose statements have been confirmed by Tieffenbach, O. Nasse, and Naunyn. These positive statements cannot be refuted by the fact that others, such as Schiff and Ritter, found no sugar in the urine after injecting glycogen into the blood, since sugar does not pass over into the urine until its accumulation in the blood has reached to a certain extent. According to Schiff [(d) and (e)], the ferment does not form in the blood until after death, or, during life, as the result of some derangement of the circulation, even a retardation of the current sufficing to produce it; and he explains the different kinds of mellituria, as well as diabetes mellitus, as due to vaso-motor derangements which give rise to the formation of the ferment, and consequently

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ligation of the portal vein, yielded contrary results, but they have no bearing upon the question stated above, since no attention was paid to the animals' feed or to any glycogen which may have been present in the liver.

[1] Experiments undertaken with reference to this point by *Pink* and *G. Heidenhain* seem to tell in the contrary direction, but they are not sufficiently conclusive.

to the conversion of the glycogen into sugar. This hypothesis is disproved by Pavy, who performed numerous experiments with all sorts of interference with the circulation, without mellituria being produced; moreover, it is contradicted by a fact, for our knowledge of which we are indebted to Schiff himself, namely, that in hibernating frogs, whose livers contains glycogen, but no ferment, the sugar-puncture is unsuccessful, although it produces quite decided disturbances of the circulation. That the ferment is not present in the hepatic cells, but in the blood, is also supported by Naunyn's (and Nencki's) examination of the liver of an artificially diabetic animal, after having injected it with an ice-cold solution of common salt, after which no sugar was found. According to the most recent investigations by Tiegel and Plósz, it is in the highest degree probable that, if the red blood-corpuscles perish, as undoubtedly happens in the liver, this ferment is developed in special abundance.

Accordingly, we must, in the present state of science, regard the processes in the liver, in so far as they now come under consideration, in this wise: that, in its cells, the glycogen-producers (sugar, glycerine, gelatine, and probably albuminates) are converted into glycogen, and that the latter is transformed into grape-sugar by reaction with the blood which bathes the cells. It is at present uncertain whether all the glycogen is gradually changed into sugar, or only a part of it, whilst the other portion serves the remaining purposes of nutrition, the formation of bile, etc. Partly because of the low diffusibility of glycogen, whereby its passage into the circulation is hindered, and partly because the newly formed sugar is at once carried away with the blood, and, under normal conditions, used up in the body, only small quantities of sugar are ever found in the liver and even in the blood.

The reaction between the cells and the blood takes, of course, a certain length of time. If this be shortened by acceleration of the entero-hepatic circulation, and time enough be not afforded the cells to take up and elaborate the glycogen-producers contained in the portal blood, or if a disproportionate amount of these substances be carried to them in the course of a short time, the necessary result is that more or less of it passes unchanged through the liver into the general circulation, and, if its quantity exceed a certain limit, from thence into the urine. This explains the mellituria which occurs when sugar is carried into the portal vein, or simply into the intestine in large quantities at a time, and likewise many cases of the so-called artificial diabetes, *i. e.*, those produced experimentally, of which there is already a great number.

At the head of all these methods, both for certainty of success, and, in particular, for its significance as regards the doctrine of the physiological and pathological formation of sugar, stands the *sugar-puncture*, taught by Bernard. This consists, as is well known, in delicately wounding the fourth ventricle with the point of a needle, on the floor of the fossa rhomboidea, immediately above the point of origin of the vagi nerves. Bernard soon became convinced that the result of this injury was not, as he had at first supposed, dependent upon an irritation of the vagi, since section of these nerves in nowise altered it. On the other hand, he found the sugar-puncture ineffectual after division of the splanchnic nerves, and he thence concluded that the channels through which the appearance of sugar in the urine was caused by the medulla oblongata ran through them. Bernard's experiment with the sugar-puncture has been confirmed hundreds of times. Our further knowledge of the course of the nerves governing the formation of sugar, and the nature of their action, we owe to the researches undertaken by Schiff, Pavy, Eckhard, Cyon, and Aladoff.

Schiff [(b) and (d)] observed sugar in the urine also on section of the optic thalami and the great crura cerebri, and on destruction of the pons Varolii and the middle and posterior crura cerebelli. Under favorable circumstances he was able to produce excretion of sugar in the urine, lasting for a week, by complete division of the spinal cord at the level of the second dorsal vertebra; often, also, by section of the individual columns of the cord (sometimes the posterior, at other times the anterior); and lastly, too, by destroying the spinal cord in its lumbar portion, so that all the nerve-connections of the liver were spared.

Pavy saw the urine become saccharine within an hour after section of the medulla oblongata, artificial respiration being kept up. Section of the crura cerebri, however, or of the spinal cord between the second and third cervical vertebræ, and from there down, he found ineffective. In regard to the sympathetic nervous system, his experiments showed that injury of the vertebral plexus of the sympathetic, or destruction of its uppermost cervical ganglion, as well as division of the nerve-filaments which ascend from the upper thoracic ganglion to the cervical canal on either side of the neck, was sure to render the urine highly saccharine, but that section of the last-named connecting fibres on one side only, as well as injury of the thoracic portion of the sympathetic below the uppermost ganglion, was feeble or uncertain in its effect; and, finally, that division of the carotid portion of the sympathetic was of no effect whatever. Pavy also divided all the nerves entering the liver from the lesser epiploon, carefully sparing the vessels, but was unable thus to produce any mellituria.

Eckhard was unable to give rise to mellituria by destruction of the uppermost cervical ganglion, but he did produce a highly pronounced mellituria by destruction of the lowermost cervical ganglion (the one which comes next after the ganglion stellatum), and a scanty excretion of sugar by destruction of the first and second thoracic ganglia, and often by section of the last cervical or the first thoracic nerve. He found furthermore that, in rabbits, injuries of the posterior lobe of the vermiform process of the cerebellum were followed by hydruria and mellituria; and lastly, he confirmed Bernard's statement in regard to the effect of division of the splanchnics. After the latter, all those injuries of nerves which caused excretion of sugar were ineffectual, no matter in what part of their course the section had been made. Carbonic oxide diabetes was not prevented by division of the splanchnics in dogs.

Finally, Cyon and Aladoff likewise found mellituria in dogs, after section or careful extirpation of the lowermost cervical or the uppermost thoracic ganglion, as well as after division of the two vertebral branches or of the two nerve-filaments leading to the stellate ganglion and forming the ring of Vieussens around the subclavian artery. Previous division of the dorsal gangliated cord of the sympathetic between the tenth and twelfth ribs, or of the splanchnic nerves, prevents the excretion of sugar from extirpation of the lowermost cervical ganglion. But, if the excretion of sugar have already begun on account of the extirpation, subsequent section of the dorsal gangliated cord of the sympathetic does not cause it to disappear. The same is true of division of the splanchnics. They explain this state of things in this wise: that by the previous sections other extensive vascular districts are paralyzed and over-distended with blood, so that the sugar-puncture or other procedures can no longer exert any influence upon the amount of blood in the liver, whereas the case is otherwise if the increase of blood in the liver and the mellituria have already begun before the sympathetic or the splanchnic is cut through.[1]

Although these experiments do not agree with each other in every particular, this much may be deduced from them: that injuries of the medulla oblongata, of the lowermost cervical and uppermost thoracic ganglia, and of certain connecting filaments of the two, give rise to mellituria. Statements in regard to the occurrence of mellituria after injuries of other portions of the central or sympathetic nervous system are in part contradictory and in part too desultory, and hence need further confirmation. Amongst these belong Schiff's observation, that sugar appears in the urine after division of the nerve-trunks of the limbs—the sciatic, for instance, and those of Munk and Klebs (in opposition to Eckhard), that the same is the case after extirpation of the solar plexus. Schiff succeeded also in causing mellituria in rabbits by thrusting long needles through the skin into the liver and moving them about within it for a short time, or directing a galvanic current through them into the liver. He explains the effect of this, as of all other procedures, by the hyperæmia which it causes directly or indirectly, and which gives rise to the formation of the sugar-producing ferment, which, in his opinion, is otherwise not present during life. Similar processes would seem to lie at the root of diabetes mellitus, but his view, as to the formation of ferment not taking place until after death, has been shown above to be untenable.

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[1] In regard to the occurrence of mellituria after section of the splanchnic, which was observed by *v. Graefe* and *Hensen*, and occasionally by *Ploch* also, compare *Eckhard*, loc. cit., p. 7.

Of other methods of producing mellituria, we must first mention, as quite directly connected with the circulation and the state of the blood in the liver, the injection of defibrinated arterial blood into the portal vein, recently reported by Pavy [(d)]. Venous blood does not seem to have this effect. In consideration of this, as well as of the effect of certain poisons, under which, as after section of the sympathetic, the vessels become dilated and allow the blood to flow through without being disarterialized, he is at present of the opinion that diabetes in man depends upon a (paralytic) dilatation of the blood-vessels in the liver.

In this connection there is a great range of substances which, whether introduced into the general blood-current or into the portal circulation, cause mellituria with more or less certainty. The oldest and best known of these agents is curare, and of like effect is poisoning with carbonic oxide (Bernard), with *chloride of carbon* (Eulenburg), nitrite of amyl (F. A. Hoffmann), nitrobenzole (Ewald), phosphoric acid (Pavy), turpentine (Almén), corrosive sublimate (Rosenbach), nitrate of oxide of uranium (Leconte), etc. Bock and Hoffmann produced mellituria by injecting large quantities of a one per cent. solution of common salt into the veins ; Kuelz, with solutions of carbonate, acetate, valerianate, and succinate of soda ; Kuentzel, with solutions of carbonate, phosphate, and hyposulphite of soda or of gum arabic. Harley observed temporary mellituria after injecting ether, alcohol, or ammonia into the portal vein, and G. Goltz, in rabbits, after injecting large quantities of lactic acid into the stomach.

According to Reynoso,[1] disturbances of respiration, whether from mechanical impediments or from the action of certain gases, such as chloroform, etc., would seem to cause glycosuria, and for the particular reason that sugar is excreted if its combustion in the lungs be prevented. His statements have, however, been proved to be exaggerated, at least they have not in their entirety been confirmed either by clinical observation of patients with the most diverse disturbances of respiration, or by experimental investigations (Frerichs and Staedeler,[1] and Senator[2]). Probably in most of the cases the reactions of the urine attributed by Reynoso to sugar were due to other reductive constituents. But, at all events, sugar does appear in the urine in many cases in connection with respiratory disturbances, and in that event probably one or the other of the processes, presently to be mentioned, comes into play.

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[1] Annales des sciences naturelles. 1855. p. 120, and Comptes rendus. XXXIII. and XXXIV.

To begin with, we must give up the attempt to find a general explanation which shall hold good for all sorts of mellituria—observed after one or another procedure, after injection of this or that agent, and not constantly at that. It would, indeed, in the present state of our knowledge, be a vain endeavor to seek after the causes of the mellituria occasioned by agents of whose physiological action we know so little, as, for instance, corrosive sublimate, turpentine, or the salts of uranium; or to examine why, as in poisoning with morphia or strychnia, mellituria sometimes forms a part of the multifarious train of symptoms (Pavy, Bernard). But, even if, out of all the methods of procedure enumerated, we consider only such as act under apparently the more simple conditions, and, for that reason, with greater certainty, it may still be doubtful whether in those cases the mellituria is always brought about in the same way. Many of the procedures mentioned—probably most of them—have this in common, that they occasion an *overfilling of the liver with blood.* That this is caused by Pavy's injection of blood is, of course, beyond all doubt; that curare and nitrite of amyl act in the same manner, we may with equal certainty assume from their known physiological effect, and so, with more or less probability at least, of many other agents. Direct mechanical irritations of the liver, too, injections of irritating substances into the portal vein or the digestive canal, may or must cause at least a hyperæmia of the liver. It has been a matter of dispute whether these injuries of nerves really cause mellituria by paralysis of vaso-motor nerves, *i. e.*, by paralytic dilatation of vessels, or whether an irritation, probably specific, of the nerves which govern the formation of sugar is occasioned by them. The latter supposition seems to be chiefly favored by the fact that the excretion of sugar is for the most part only transitory, which may be explained by the cessation of the irritation. But since the existence of actively dilating nervi vasorum was conclusively ascertained by Fr. Goltz, there has been no ground for this dispute. Whether the injury of the nerves acts by irritation or by paralysis, we may in either case explain the dilatation of vessels in the portal domain which is quite directly observed after dividing certain nerves.

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[1] Verh. der naturf. Ges. in Zürich. III. and Mueller's Archiv. 1854. p. 393.

[2] Virchow's Archiv. XLII. p. 1.

Dilatation of the hepatic vessels, when not occasioned by impediments to the outflow, by venous stasis, causes an acceleration of their current of blood, by reason of which, as has already been mentioned *passim*, the contact with the glycogen-forming hepatic cells is abbreviated, and the transition, unchanged, of the sugar or other glycogen-producers brought by the portal vein is favored. The action of the hepatic cells is, as Luchsinger has shown, in nowise altered as regards its kind, only the relative quantities of material brought to them (to be elaborated by them) and carried away from them, and of the sugar already formed, are changed. The occurrence of mellituria under these circumstances, *i. e.*, acceleration of the portal circulation, will accordingly be dependent upon the stock of glycogen present in the liver and upon the ingestion of sugar or other glycogen-producers. The largest amounts of sugar must appear in the urine when, for instance after the sugar puncture, poisoning with curare, etc., sugar is introduced into the intestine or the portal vein, since a portion of it passes through the liver without further ado, and the other (abnormally small) portion goes to the hepatic cells, and is there changed into glycogen, to escape from them by diffusion, to appear again as sugar, and to be quickly washed away. Lesser degrees of mellituria are observed when other glycogen-producers, such as glycerine, enter the portal vein, because only a portion of them is changed into glycogen and then into sugar, whilst the other portion is carried away without undergoing the action of the hepatic cells, more especially if, without any fresh accession, the liver still contain glycogen as the result of previous feedings. On the other hand, the sugar puncture and other methods, which ordinarily cause mellituria, do *not* effect this any longer, if the liver have become free from glycogen by long fasting, and no fresh addition take place. But, if the hepatic cells have suffered impairment of their functional capacity, at least as regards the formation of glycogen, as by fatty degeneration, and if the stock of glycogen in the liver be exhausted, then mellituria cannot occur except sugar gain access to the intestine or the portal vein. It will then pass unchanged through the liver into the general circulation. All these facts have been established by Luchsinger in particular, and have led to a knwloedge of the views here laid down.

In this way the great majority of cases of artificial diabetes find an explanation which is not forced, and which tallies with the most recent investigations. Many of the statements of experimenters which seem to conflict with it, especially in former years, are readily explained by their ignorance of one or other circumstance, the significance of which has not been made clear until now, as, for instance, the nutritive condition of the animals employed in experiments, or the composition of the material which is carried to the liver, etc. Even Pavy's experiment, already quoted, of collective ligature of the hepatic nerves without mellituria occurring, cannot be held valid as proof against this theory, since no attention was paid to the glycogen contained in the liver. Moreover, a repetition of this experiment, which, indeed, is scarcely in accord with the most recent views of Pavy himself (p. 942), is much to be desired.

But there are still many forms of artificial diabetes which cannot be satisfactorily explained in the foregoing manner, because in them a participation of the liver, such as is required for the other forms, cannot be shown, or can only be assumed by straining the natural interpretation of the evidence. This applies to the mellituria which Schiff says that he observed after division of the lumbar spinal cord, or of various peripheral nerve-trunks; and partly also to the mellituria which occurs after injections of dilute solutions of different salts into the vascular system, and which Bock and Hoffmann ([c] p. 40) saw take place, too, some time after extirpation of the liver; and finally to still other forms of mellituria. Are we justified, on this account, in rejecting as false the doctrine which has been presented, of the function of the liver in forming glycogen and sugar, and of the part played by dilatation of the vessels—a doctrine which is abundantly supported by collateral facts? Certainly not. Rather, if there be cases of mellituria which do not, to be sure, contravene this doctrine, but yet are not explained by it, it follows that there must be still other causes of mellituria, unconnected with the liver—causes which must concern either the ingestion or the formation, or the appropriation and excretion of the sugar and of the glycogen which is so closely related to it.

Thus far we have never fully grasped all these causes, but have pursued but the one or the other of them, being prejudiced by the prevailing current. During the earlier period, for instance under the overpowering impress of Bernard's discoveries, research directed its entire attention to the *sources* of the sugar, and, among these again, almost exclusively to the liver. Whilst the part played by the liver under all imaginable conditions was investigated experimentally, the study of the other conditions which may claim consideration, in connection with the excretion of sugar, was unwarrantably neglected, not merely as regards the explanation of the various sorts of glycosuria which may be produced artificially, but, *à fortiori*, as regards the theories of *diabetes mellitus.*

The theories which have attracted most attention have already found their place in the foregoing exposition; the others hinge, some of them rather upon Bernard's, and others, and the most of them, upon Pavy's view of the function of the liver, and they modify or enlarge these views in one way or another to explain the disease. Seegen discerns the essence of diabetes in a morbid transformation of the glycogen of the liver, occasioned in most cases by a disturbance in the tract of the nervous centres. He is inclined to refer the different "forms" (or stages) of the disease to differences in the hepatic glycogen, according as it has proceeded from the hydrocarbons or from the albumen of the food; and he finds a prop for his view in a statement of Schtscherbakoff's, who avers that he has found various modifications of the glycogen of the liver. This support has been shaken by the opposing statements of Luchsinger, Salomon, and Kuelz, and, besides this, the correctness of his view must remain doubtful so long as the development of glycogen from albumen is itself a matter of doubt, or else we must consider only the gelatine of the albuminous food (compare p. 935). A similar exposition has been brought forward by Cantani, and likewise by Foster; they conclude that at least certain cases of diabetes depend upon the formation of a sort of sugar (paraglucose) different from the ordinary hepatic sugar, and incapable of oxidation as such within the system. In other cases, according to Foster, the liver would seem to have lost the power of retaining the sugar as glycogen; and in still others, the severest, an immoderate action of the liver would seem to take place, which then forms sugar even upon an albuminous diet. Dickinson, who likewise does not question the normal formation of sugar by the liver, together with that of glycogen, attributes the disease in all cases to an augmented accession of sugar to the blood, since there is nothing to indicate a diminished consumption of sugar, if it be added to the blood in normal quantity. The increased accession may depend: first, upon an *excess of sugar in the food*, which at once simply passes into the blood, and causes a temporary glycosuria ("normal alimentary glycosuria"), which disappears on diminishing the saccharine food; second, upon a *lack of power in the liver to form glycogen out of sugar and starch*—this seems to have occurred in those slighter cases of diabetes, or in the first, imperfect stage, in which the excretion of sugar is stopped by withdrawing the hydrocarbons ("abnormal alimentary glycosuria"); third, and lastly, upon an *increased formation of sugar* in the system occurring independently of the ingestion, as takes place in the severer cases of diabetes. In this connection may be mentioned also many cases in which either an abnormal amount of glycogen is developed, or, which is quite improbable, however, an unnatural proportion of it is changed into sugar by a morbid formation of ferment, or in which sugar instead of glycogen is formed in the liver. Dickinson believes that we cannot assume that an abnormal quantity of glycogen is formed, and that, too, in consequence of a hastened circulation, because the function of a hyperæmic organ is never simply increased, but always altered in quality;[1] accordingly, the most probable hypothesis is, *that diabetes mellitus is caused* (in severe cases) *by a defective functional action of the liver, which forms sugar instead of glycogen from albuminous food.* Disturbances in the domain of the nervous system lie at the foundation of all these changes, whereby abnormal circulatory relations are established. However fully we are compelled to acknowledge that, in this exposition of Dickinson's, the modes in which mellituria is developed, in so far at least as concerns the liver, are more completely considered than by others, we yet cannot characterize the last conclusion as in any way a happy one. For, in the first place, no mellituria has ever yet been ascertained to have developed while the liver was free from glycogen and without the ingestion of sugar (see pp. 936 et seq.), and moreover it is in the highest degree improbable that in the lighter cases the liver should still possess the power to form glycogen out of proteine matters, but not out of sugar; for, according to all that we know, the development of glycogen from albuminous bodies, if indeed it be proved, must require much more complicated processes than from sugar.

Zimmer has broached a view which has, at least, the merit that it does not confine itself to the liver alone, but takes account of the muscles also; but it is chiefly supported by mere conjectures, and does not comport well with a number of recently discovered facts. According to him, the cause of diabetes may lie in the liver or in the muscles, and the latter are implicated particularly in the severer cases. The liver and the muscles contain glycogen, ferment, and water, and upon these three factors depends the formation of sugar. The amounts of glycogen and of ferment remain relatively constant, that of the water being variable. If the latter be permanently increased, so that a continuous formation of sugar takes place in these organs, then diabetes mellitus is developed. If by paralysis of the vessels, such as takes place in the liver upon well-known nerve-injuries, a greater diffusion of water in the organ is brought about, the same may occur likewise in the muscles after division of their nerves, chilling, etc.

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[1] This cannot be conceded as a general proposition. A distinction should be made between venous hyperæmia (stasis) and active hyperæmia (fluxion, orgasm), and it is known that in the latter abnormal constituents do not necessarily appear in the secretions. In support of his conclusion, Dickinson alleges that in curare-poisoning mellituria occurs without the formation of glycogen; but, as Luchsinger has proved, this is not correct.

Pettenkofer and Voit concluded, from their very instructive researches upon the interchange of matter in a diabetic (see p. 926), which indicated a relatively small absorption of oxygen, that there was, therefore, a disproportion between the destructive process and the absorption of oxygen ; that this was occasioned by the greater proneness of the organic albumen to destruction in the diabetic, owing to its greater lability, which seemed to them to be rendered probable by many disturbances which occur in the course of the disease. The fact that the absorption of oxygen does not correspond with the destruction, they explain by a diminution of the number of the red blood-corpuscles or their power to fix oxygen, in consequence of which, too, the destructive metamorphosis within the body does not advance to its normal final products, but pauses at the production of sugar. In opposition to this theory, it has rightly been urged that the diminished absorption of oxygen may be the result as well as the cause of the imperfect oxidation and of its arrest at the stage of sugar, and that the greater lability of the organs which excrete sugar follows only after a length of time, and does not precede it, as would have to be the case according to that theory.

From a similar standpoint, Huppert and Gaethgens (see p. 899) had previously indicated an increased decomposition of albumen as the essential feature in diabetes mellitus, and Lecorché also adhered to this view. Huppert imagines that the organic albumen is not made use of in diabetics, as it is normally, to form blood-corpuscles, but is decomposed in greater quantity in the organs themselves, and, on account of the diminished oxidation, only into urea and sugar. But it has already been pointed out that a *specific* increase of the excretion of urea is not by any means generally present in diabetes, and, moreover, it is difficult to bring this theory into consonance with the fact that the excretion of sugar is diminished or entirely stopped by animal diet, in spite of an increasing excretion of urea.

Besides the theories which have been quoted, numerous others are to be met with in literature—some of them but hastily thrown out, others founded upon more or less detailed observations of the disease; but we forbear enumerating them, because they have either been rendered obsolete and untenable by the progress of investigation, or contain nothing essential which is not included in the expositions already adduced.[1] That not a single one of these theories has thus far obtained general recognition is the less to be wondered at, since they all proceed from a one-sided comprehension of the disease. Where pathology and anatomical and clinical study still offer so few fixed points, and leave so much room for the play of conjecture, as is the case in regard to diabetes, we cannot yet undertake to set up a complete theory which shall be proof against all cavil, but must seek out provisionally *all* the conditions under which the characteristic morbid phenomena—in this case, therefore, the mellituria—may appear, and give prominence to those which possess the most *probability*. We shall thus be sure to be right in all cases, and we shall, moreover, be preserving guide-boards to the paths which further research will have to follow.

Ordinarily no sugar passes out of the blood into the urine—at least, not enough to be detected with certainty. Bruecke[2] has stated, to be sure, as is well known, that normal urine contains sugar, although in mere traces, and there has been a good deal of contention for and against this statement; but the question has now been settled by Seegen[3] in this wise: that our present methods are not sufficient to positively detect sugar in ordinary urine, and that, when sugar does seem to be contained in it, it must amount to not less than 0.01 per cent. But this does not by any means prove that every excretion of sugar in the urine is a pathological phenomenon, and still less that in every such case we are dealing with a diabetes mellitus. On the other hand, we shall come to know of causes for the excretion of sugar which either lie quite within the limits of health or stand upon the very boundary-line between physiological and pathological conditions, but in regard to which there can be no question of a diabetes mellitus.

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[1] The theory maintained by *Schultzen*, that the diabetic excretes sugar because he is deficient in the ferment which normally changes the sugar into glycerine and glycerine-aldehyde, is destitute of any foundation in fact. Compare *Kuelz's* criticism of it (Deutsch. Arch. f. klin. Med. XII. p. 248).

[2] Sitzungsber. der k. k. Acad. zu Wien, 1858. XXVIII. p. 568, and 1860, XXXIX. p. 10.

[3] Ibid. 1871. LXIV. Juin.

The passage of sugar out of the blood into the urine may follow either from the normal amount of sugar in the blood being exceeded, or from the sugar being, on account of an altered condition of the blood or of the tissues seated between the blood and the urine, no longer held back, as it normally is. Again, an unnaturally large amount of sugar in the blood may be occasioned (A) by *an augmented accession* or (B) by *diminished consumption* of sugar.

How high the saccharinity of the blood must rise before an obvious mellituria takes place, we cannot say with certainty, because in experimental researches upon this point many circumstances conspire to cause variations in the separation. Becker saw mellituria in rabbits after injecting 0.5 per cent. of sugar into the blood (Lehmann and Uhle, after 0.6 per cent.), but, following the sugar-puncture, after 0.357 per cent. According to Bernard, mellituria occurred in dogs after injecting from 0.25 to 0.3 per cent. Probably, therefore, individual conditions also come into play.

A. *The access of sugar to the blood* may be increased in three ways, namely: I. From the intestine; and that, too, either (a) directly, through the lacteals, or (b) circuitously, through the liver. II. From the muscles. III. From the secreting milk-glands, by absorption into the blood of the sugar of milk formed in them. This includes all known sources of sugar.

I. *Increase of the Saccharinity of the Blood from the Intestine.*

(a) *The chyle* contains small quantities of sugar which, of course, proceed exclusively from the sugar introduced into the intestine or formed within it from starch. This is not contradicted by the fact that Colin, Chauveau, and Bérard detected saccharinity of the chyle, and that to a very slight degree, after feeding with meat, for this may be explained by the fact that meat contains hydrocarbons. An increased access of sugar by way of the chyle can be caused only :

First, by an abnormally large ingestion of starch or sugar with the food. That mellituria may thus be developed has been repeatedly observed in man and beast. (Compare pp. 868 and 938.) This sort of mellituria ceases upon discontinuing the ingestion of sugar, and has no pathological interest.

Secondly, by an abnormally heightened transit of sugar from the intestine into the lacteals (even without increased ingestion). According to the view generally accepted, the sugar present in the stomach is changed, more or less of it, into *lactic acid*, and the unchanged remainder is absorbed by the lacteals and the radicles of the portal vein. Now, many variations suggest themselves here, which may increase the saccharinity of the chyle, and thereby that of the blood. It may be that in consequence of *abnormal digestive processes the conversion of sugar into lactic acid is more or less restricted*, so that the sugar is absorbed as such in greater quantity than usual; or *the conditions may be more favorable for its imbibition*, so that there is not time enough for the conversion to take place within the intestine; or, finally, owing to some impediment or other in the portal circulation, the absorption of sugar, in which both vascular systems usually take part, falls wholly, or to an unnaturally great extent, to the lacteals. Which of these possibilities actually comes into play, and under what circumstances, thus lying at the foundation of mellituria, we can at present only conjecture, at the most, but cannot say positively or even with bare probability. But there are facts enough at hand to prove that the processes here mentioned should not be ignored, as is the case in the present bent of pathological and physiological investigations of diabetes. That famous case of Andral's,[1] *in which mellituria had existed with complete obliteration of the portal vein, as proved on post-mortem examination*, although passed over in silence almost everywhere in recent literature, may yet well direct our attention to the possibility that an abnormal amount of sugar may be taken up in the chyle in one or another of the ways here mentioned. To the most recent period, and to its therapeutic endeavors, we owe certain other allied facts. One of these is the favorable effect of *lactic acid*, first announced by Cantani, and often found correct by others. This acid, as Scheremetjewsky has shown,[1] is entirely oxidized in the blood; that is to say, it is used up there and becomes a source of power, which does not occur in the same way with the grape-sugar which finds its way into the blood. We may therefore well imagine that the acid serves a useful purpose in cases in which the development of lactic acid in the intestine is restricted. The other fact consists in the varying influence of the hydrocarbons upon the excretion of sugar in diabetics, even of such hydrocarbons as have been shown by experiments on animals to be fertile sources of glycogenesis in the liver. According to Luchsinger and Salomon, *inuline* and *levulose* (fruit-sugar) increase the amount of glycogen in the liver, but, as Kuelz has observed, they may be taken by various diabetics with impunity, *i. e.*, without any effect upon the proportion of grape-sugar in the urine. *Sugar of milk*, also a glycogen-producer, sometimes behaves in the same way, and since Schultzen pointed out the effects of *glycerine* in diabetics some cases have been observed in which the quantity of sugar in the urine was increased by saccharine and farinaceous food, but not by glycerine (see "Treatment"). All of which amounts to this, that the cause of an abnormal saccharinity of the blood may reside in some other organ than the liver. Such cases can scarcely be explained otherwise than by supposing that the *grape-sugar*, which is ingested or formed out of starch, remains wholly or in great part unchanged, owing to anomalies in the primæ viæ, gains immediate access to the blood through the chyle, and so increases the amount of sugar in the urine. The *other hydrocarbons*, on the other hand, except possibly sugar of milk, when they gain access to the blood in the same way and unchanged, can exert no influence upon the amount of sugar in the urine, but may simply pass through the blood or be oxidized in it. But it is not improbable also that they behave in various ways in the intestine itself, in accordance with different conditions of solubility and other chemical peculiarities—remaining unaltered for a shorter or longer time, or being absorbed before their conversion is completed.

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[1] Comptes rendus. 1856. XXXIV. p. 468.

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[1] Sächs. acad. Sitzungsber. 1869. p. 154 et seq.

Finally, those symptoms so common in diabetics, which point to an implication of the gastro-intestinal canal, but not to the liver, should not be undervalued. The existence, in many cases, of digestive derangements, before the outbreak of the disease and during its development, favors the assumption that we are sometimes dealing with departures from the ordinary behavior of the starch and sugar ingested; especially is this true of the fact that diabetics very commonly not only consume immense quantities of food, but also digest it with surprising rapidity, that their sense of satiety seems almost wholly lost, and that this is particularly observed under the use of farinaceous and saccharine food. This fact seems indeed to point to an abnormally rapid removal of the sugar from the stomach and intestine, probably by absorption.

Falck, to be sure, observed, as has before been mentioned (p. 895), a slower excretion of the ingested water through the kidneys in diabetes mellitus (and insipidus) than in health, and he attributed this fact, which was confirmed by Neuschler and Kuelz, to a *retarded* absorption of water. But, apart from the fact that there are other ways of explaining this, it has been found by Neuschler that in *sugar*-diabetics (in contradistinction to those suffering from diabetes insipidus!) *the absorption of water is actually hastened by giving highly amylaceous food, especially bread.* Falck himself found absorption stimulated by grape-sugar, whilst Griesinger found cane-sugar more efficacious in this respect than grape-sugar.

All these facts, to say nothing whatever of the most efficacious methods of treatment, which might here be quoted to the same purpose, point too decidedly to disorders of gastric and intestinal digestion to allow of our wholly overlooking them in favor of the so-called liver theory of diabetes. From Rollo to Bouchardat, men have sought for the source of the disease in gastro-intestinal derangements, and a *gastro-intestinal theory* has even been set up, but has had to yield before our advancing knowledge of the processes of digestion. However, what has recently been brought into consideration in regard to the digestive processes in diabetes is limited to the functions of the pancreas, by default of which sugar would seem to be abnormally developed. The numerous cases of disease and atrophy of the pancreas without diabetes sufficiently contradict this otherwise lame theory. According to Klebs, the striking frequency of pancreatic affections in diabetes is best explained by concomitant changes in the cœliac plexus, which give rise to mellituria and lesions of the pancreas as co-ordinate effects (compare p. 888).

It is not yet time to set up any new gastro-intestinal theory, but it is time to pay more attention to the gastro-intestinal processes in diabetes, which have hitherto been quite thrust into the background. In particular, the varying behavior of individual cases, under certain dietetic and medicinal methods of treatment, might, if further followed up, promise an explanation of the derangements of digestion in one or another sort of diabetes.

b. We may imagine an increased access of sugar to the blood dependent in various ways upon the *liver*. *In the first place*, it may, as a result of mere increase of action, form more sugar out of glycogen, and for the simple reason that more of the producers of glycogen are ingested with the food, or that more of them than natural reaches the portal vein, or because from other causes more glycogen than normal is changed into sugar.

We can scarcely consider the simple increase of the hepatic glycogen, in consequence of augmented ingestion of food, as the general cause of an increase of sugar, for the mellituria continues, even if it finds access to the intestine in normal amount. But just here we must insist again upon the possibility *that, on account of changes in the digestion or in the state of the circulation in the intestine, an abnormally small proportion of sugar is transformed into lactic acid, and that therefore an unnaturally large quantity of it passes into the portal vein as well as into the chyle* (p. 952).

But, if the access of glycogen-producers from the intestine and the portal vein be normal, yet for some reason or another there may go on in the liver itself a more rapid transformation of the glycogen which is formed in normal amount. Many have sought to find the reason for this in the fact that an abnormally large amount of *ferment* is formed, and that *thereby* an unusually large quantity of glycogen is changed into sugar. There is not much in favor of this opinion, however, for, in the first place, according to our ideas in regard to ferments, it is not at all necessary that, for the conversion of more material, more ferment should be present; on the contrary, we are accustomed to see the transformation go on almost ad infinitum with a relatively small amount of ferment; and, in the next place, the fact that glycogen has been found persisting in the dead bodies of diabetics (see p. 893), that is to say, for a greater or less length of time after death, during which the conversion into sugar goes on even more briskly, does not indicate a specially augmented action of the ferment. It accords much better with our ideas to assume, *that the hepatic cells do not retain their glycogen as they normally should, and for the very reason that the circulation in the liver is hastened, and that large quantities of blood, and therefore of ferment, are enabled to come in contact with the cells in a given length of time.*

Secondly, the capacity of the liver to transform into glycogen the sugar which is brought to it from the intestine (and to retain it in the cells) may have been wholly destroyed, or may be incompetent in proportion to the quantity brought to it. I hold it to be very improbable that the liver of a diabetic is wholly incapable of preparing glycogen, because, as has already been mentioned, in the first place, glycogen is found in the dead body; and, further, because we not infrequently see the excretion of sugar increased by glycerine, which may well allow us to conclude that it was previously changed into glycogen; then, because, in all sorts of *artificial* mellituria which have been investigated in regard to this point (from the sugar-puncture or from poisoning with curare), the liver continues to form glycogen; and, finally, because the hepatic cells, which are the particular seat of the formation of glycogen, are not by any means destroyed in diabetes, but rather hypertrophied, and their further function, too, *i. e.*, the formation of bile, is not, according to all that we know, impaired in diabetes; nevertheless, we cannot with absolute certainty exclude the possibility that, in this or that case, the power of the liver to change sugar into glycogen has been wholly destroyed.

It is much more likely that the activity of the liver in forming glycogen is not sufficiently powerful, *i. e.*, does not suffice to transform the whole amount of sugar which is brought to it in normal or abnormal quantity (p. 956), and that, too, primarily, *again, because the current of blood within it is hastened, and consequently a portion of the sugar reaches the general circulation unchanged, without having undergone the action of the cells.* This pathological process, in connection with the more rapid transformation into sugar of the glycogen simultaneously formed, may be considered as perfectly parallel with the mellituria occasioned by the sugar-puncture, in which the animals continue to form glycogen (see p. 936).

Thirdly, we must consider whether the liver does not form sugar in diabetes, no matter whether with or without the previous formation of glycogen, from materials out of which normally no sugar is developed. The oft-repeated observation that there are diabetics who excrete sugar, even upon an exclusively animal diet, was long ago brought to bear upon the question of whether in such cases (glycogen and) sugar were not developed from albumen, and certain experiments in the feeding of animals (see above, p. 935) seemed to answer this question in the affirmative, and to furnish a clue for the explanation of those severe cases of diabetes. Many have thought, and still think, that in these cases the liver makes use of a power which otherwise it employs only exceptionally, in case of necessity, as it were, when, for instance, no hydrocarbons are furnished to it. But, now, the formation of glycogen and sugar out of pure albuminates has recently been rendered doubtful; only one *albuminoid*, gelatine, has been certainly proved a producer of glycogen, and, remarkably enough, the chemical production of saccharine matters outside the body has thus far been achieved with it alone, but not with the true albuminates. But thus the sole support of this view is shaken. Furthermore, a pure animal diet, even the so-called "exclusively meat diet," does not consist of albumen alone, but contains glycogen also, as well as undoubted glycogen-producers and hydrocarbons in quantities which are not to be disregarded, namely, besides *glycogen* and the *meat-sugar* which apparently proceeds from it, also *gelatine*, *glycerine* (in the fat), and lastly *inosite*, of which, to be sure, the capacity to form glycogen has not thus far been investigated. We may estimate the amount of these substances at from three to five per cent., even in meat which is poorest in them, but it commonly amounts to decidedly more. Add to this that, in the most stringent diet lists for diabetics, in addition to the meat, are to be found butter and fats of all sorts; eggs (containing considerable fat, with grape-sugar and perhaps glycogen also), and all kinds of vegetables; that the drinks which are allowed even in the severest cases, tea, coffee, and wine, are not absolutely free from sugar and sugar-forming elements; and we shall have to allow that, even with the most rigorous diet, but which, with or without the physician's knowledge, is never, as is well known, persistently carried out, some hundreds of grammes of sugar and sugar-producers are eaten daily. If we compare therewith the quantities of sugar excreted in the severe and severest cases of diabetes, in which, moreover, milk, very small amounts of amylaceous substances, and the like, are still commonly enough allowed, we shall find that, with very few exceptions, the latter fall far short of the sugar and sugar-forming elements ingested, and that, therefore, there is thus far no necessity of assuming a formation of sugar out of albumen. Bock and Hoffmann ([c] p. 68) looked through the literature (with another view), and found only two cases in which more than two hundred grammes of sugar were excreted upon a nominally pure meat diet;[1] and they correctly add, that it is well worth thinking of, whether these figures are absolutely correct, for, according to their experience, in which most physicians would probably agree, the excretion of sugar is always reduced to a minimum by positive exclusion of all "hydrocarbons" from the food, *i. e.*, except those ingested with the meat diet. *So long, then, as it is not proved that diabetics excrete sugar upon a diet free, in the strictest sense, from glycogen and glycogen-producers, and that, too, for a length of time, since at the first, indeed, glycogen developed from other substances may still be present in the liver; and so long as the development of glycogen in animals under the same circumstances is not positively demonstrated—we must reject the view that certain diabetics form sugar out of albumen, and that they are thus to be distinguished from other diabetics.* We shall find a difference in this only, that they can no longer make use of even the smallest amounts of hydrocarbons and glycogen-producers, such as are present in the so-called animal food, whilst others still assimilate such quantities. It is well known, indeed, that the latter class of patients, too, do not always void again in full quantity even the pure sugar eaten, but are capable of employing more or less of it for the purposes of the body. In the behavior of diabetics upon various (animal and vegetable) food, however important it may be in other respects—as for instance with reference to prognosis,—we can find no pervading, radical difference, but, thus far at least, only a directly advancing, quantitative dissimilarity. It is more intelligible, too, that *one and the same morbid process* may make advances, and that *thereby* one "form" or one "stage" may pass into the other, than that this transition is occasioned by an entirely new process, *i. e.*, by the formation of sugar from albumen, which otherwise does not occur.

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[1] One case was that of *Pettenkofer* and *Voit*, and the other, that of *Andral*. Another case has since been added by *Kussmaul*, in which, upon a pure meat diet without glycerine, 265 grammes were evacuated upon an average, but, as *K.* adds: "It cannot be absolutely guaranteed that the diet was adequately adhered to."

II.—According to our present ideas, we can scarcely imagine *an increase of sugar in the blood from the muscles*, other than in conjunction with and dependence upon the liver, from which they derive their sugar (and their glycogen). A mellituria, in which the muscles were the sole source of sugar, to the exclusion of the liver, could only exist for a short time, as if produced experimentally (see p. 945, and Bock and Hofmann), but could not take place as a pathological condition of long duration.

III.—The *sugar of milk, which the mammary glands* form, seems to be capable of absorption into the blood under certain circumstances, increasing its saccharinity and occasioning mellituria. At least we cannot otherwise explain the mellituria which, in spite of the opposing statements of Wiederhold (Zwengler[1]), Leconte,[2] and Griesinger, is frequently observed in pregnant and nursing women, according to the unanimous observations of Blot,[3] Heller, C. G. Lehmann,[4] Kirsten,[5] Bruecke, Hémey, Iwanoff,[6] de Sinéty,[7] and Abeles,[8] and which would seem to be increased by obstructing the outflow of milk. According to Blot and Hémey, the amount of sugar in the urine would seem to be capable of rising in this way to over one per cent. (up to 1.8), whilst Abeles estimates the quantity found by him as less than 0.02 per cent.[9] However that may be, we are here again concerned with a *physiological mellituria*, or, at least, surely not a diabetes mellitus, although the excretion of sugar may continue for a long time, through many months. Of course this does not exclude the development of a true diabetes mellitus during pregnancy or the puerperal period, as has been observed a few times. (Bouchardat, Oppolzer, and Gibb.)

B.—A *diminished consumption of sugar* was formerly often designated as the cause of diabetes, and precisely on the ground of the ideas which were then held in regard to the significance of sugar as a "respiratory and calorific substance," and its combustion in the blood. After Mialhe's theory of impeded combustion of sugar, by reason of a diminished alkalescence of the blood, had been rejected as untenable, it was in particular the above-quoted statements of Reynoso's (p. 942) which seemed to lend support to the view of a diminished absorption of oxygen, and a consequently diminished combustion of sugar. But his statements have proved untrue, and the clinical fact that the most marked disturbances of respiration, even of long duration, give rise, indeed, to mellituria now and then, but not to any real diabetes, has brought this view utterly to the ground. Even the most recent modification of this theory by Pettenkofer and Voit, who seek the cause of the diminished combustion of sugar in a defective constitution of the blood-corpuscles (compare p. 949), has acquired no recognition. The idea of an immediate combustion of sugar in the blood has been generally given up almost entirely, in consequence of Scheremetjewsky's experiments, and its use is now rather sought for in its further employment for purposes which, however, have not yet been by any means fully investigated. Only this much is certain: that the muscles use up sugar (glycogen) in their action. We might, at all events, make fast to this, were we willing to pursue the idea of a diminished consumption of sugar in diabetes mellitus; but there is thus far a lack of any further point of support, and the few facts bearing upon this matter which pathology furnishes us with do not quite favor that view. In the first place, there is the fact that, even with complete muscular inactivity in healthy persons, or in the paralyzed, no mellituria is developed, unless other causes come into play; and secondly, the fact, already mentioned, that a sudden diminution of the excretion of sugar is brought about in diabetics by muscular strain, a proof that the muscles have not suffered impairment of their *capability* of using up sugar, at least in *these* patients. Whether there are cases which behave differently, must remain uncertain until a greater number of observations have been made in regard to the influence of muscular action upon the excretion of sugar. But, however the muscles may behave, neither can we wholly dismiss the possibility that perhaps the employment *of the sugar which has reached the blood* is affected in diabetes; nay, the severer cases, those in which the excretion of sugar goes on upon a very reduced ingestion of sugar and glycogenetics, seem to point very closely to the idea that the power of assimilating and making use of sugar in whatever form, whether it be stored up as glycogen or as fat, or to oxidize it in the muscles or anywhere else—that this power is wholly lost. We might also assume that, with such diminished ingestion, more sugar reaches the blood directly from the intestine or by the circuit through the liver than in healthy persons, who are eating the usual miscellaneous diet, and that therefore those disturbances in the primæ viæ or in the liver, which were mentioned above, are here present in a higher degree. Our knowledge is not sufficient to bring us to a conclusion as to which one of these possibilities is actually at work. Each individual must rather follow his own inclination as to whether the one or the other conjecture shall be allowed as being the more probable.[1]

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[1] Ueber den Nachweis des Zuckers im Harn. 2 Aufl. Göttingen, 1859.

[2] Arch. Gén. 1857. Août.

[3] Gaz. hebdom. 1856. No. 41, and Comptes rendus. XLIII. p. 676.

[4] Lehrbuch der phys. Chemie. I. p. 270.

Monatsschr. f. Geburtsk. 1857. Juni.

[6] Beiträge zur Frage über die Glycosurie, etc. Diss. Dorpat, 1861.

[7] Gaz. Méd. 1873. Nos. 43 et seq.

[8] Wiener med. Wochenschr. 1874.

[9] *Hempel*, too (Arch. f. Gynaekol. VIII. p. 312), who confirms, in an article which has just appeared, the appearance of glycosuria in lying-in women, found in one case 1.6 per cent., and a daily quantity of 17.3 grammes of sugar in the urine.

Theoretical considerations, together with many clinical and experimental observations, tend to show that a mellituria may be called forth by *changes in the excretory relations of the sugar from increase of the blood-pressure, from variations in the composition of the blood or of the secreting tissue*, alone, and without the saccharinity of the blood being abnormally heightened. Under ordinary circumstances, it seems that it is only on account of the exceedingly slight saccharinity of the blood that no sugar passes over into the urine. By reason of the great diffusibility of sugar, however, it is probable *à priori* that even slight variations in the circulatory and pressure conditions of the kidneys, certain nutritive disorders of the walls of the vessels or of the epithelium, which heighten their permeability, and finally, changes in the blood itself, by reason of which conditions more favorable for diffusion are brought about, may give rise to a transudation of sugar into the urine. If we appeal to disturbances of this sort for the explanation of various forms of albuminuria, we may venture with still more justification to do so for one or another kind of mellituria, since indeed the diffusibility of sugar so very much exceeds that of albumen. In point of fact, there are data in regard to the occurrence of sugar in the urine which abundantly warrant these considerations. Attention has already been given to Reynoso's statements in regard to the influence of respiratory disturbances upon the development of mellituria. Even if his view has not been confirmed, that an impeded absorption of oxygen occasions saccharine urine, we must nevertheless admit that his *observations* were not wholly visionary, and that, at all events, sugar may appear in the urine in certain impediments to respiration. This is shown not only by old observations, in which we cannot reject the objection of an error due to other reductive matters, the presence of which in the urine was not remarked until later, but also by more recent investigations which are perfectly unobjectionable. To say nothing of others, Abeles (compare p. 961), who, at the instigation of Seegen, and with the utmost skepticism, examined the urine of a great number of patients, found sugar in 18 out of 66 consumptives (*i. e.*, in about 37 per cent.), and in four out of six persons suffering from valvular affections, in greater proportion than in all other patients. We might well conjecture that in these cases it was not the deficiency of oxygen, but the stasis in the kidneys due to impediments to the respiration and circulation, and perhaps also still other changes in the renal parenchyma, such as amyloid degeneration, which gave rise to the transition of sugar from the blood into the urine. The same cause may exist for the appearance of sugar in the urine in the reactive stage of cholera, as has been observed by Heintz and Samoje, Buhl, Gubler, Huppert, Wyss, and others. I myself have found sugar beyond all doubt in two out of 20 cases of respiratory disturbances caused artificially in dogs, but only on very great dyspnœa with the phenomena of considerable venous stasis.[1] Furthermore, we must probably refer the cases observed by Ollivier,[2] who saw albumen and sugar appear in the urine in apoplectic attacks with extravasations into the brain, to vaso-motor disturbances in the kidneys, and perhaps likewise many instances of mellituria in nervous diseases, such as sciatica (Braun[3]), tetanus (A. Vogel[4]), chorea magna (v. Franque[5]), and all sorts of convulsive conditions, in intermittent fever and numerous other diseases, may be explained by disturbances in the renal circulation. Finally, according to the laws of diffusion, there can be no doubt that the constitution of the blood itself may also have an influence upon the evacuation of sugar. It is known that the concentration and the composition of diffusive solutions have an effect upon the degree of diffusion and of filtration also (Nasse sen.).[1] These conditions have not yet been studied in regard to mellituria. The mellituria caused by saline injections, which occurs with a degree of saccharinity of the blood far below what is estimated as the minimal limit under other circumstances, may perhaps depend, in part at least, upon altered conditions of diffusion and filtration, and in like manner we might explain Bernard's statement that subcutaneous injection of a solution of sugar of a given concentration does not give rise to mellituria until a certain quantity of sea-salt is added. But nothing beyond these scanty facts is yet known in regard to the subject.

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[1] In a recent article (Virchow's Archiv. LXIV. p. 382), *Pawlinoff* attributes diabetes to a disease of the muscles, which are incapable of converting sugar into the easily combustible lactic acid. The facts above given are opposed also to this view, which is partly founded upon very hypothetical suppositions.

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[1] Virchow's Archiv. XLII. p. 1.

[2] Gaz. hebdom. 1875. No. 11.

[3] Lehrb. der Balneotherap. 1868. p. 343.

[4] Deutsches Archiv f. klin. Med. X. 103.

[5] Journ. f. Kinderkrankh. 1867. p. 226.

It is obvious that not every one of the conditions which have been enumerated, under which a mellituria is possible, can claim consideration in connection with the theory of diabetes mellitus. In certain cases, as was then remarked, we were dealing with purely physiological processes; other cases are, to be sure, of a pathological nature, but they lack all the other symptoms of diabetes, and, above all, the duration of the saccharinity of the urine is very brief in them, and, from the nature of the case, this must always be so. In a venous stasis, for example, but little sugar will ever pass over into the urine, so long as the ordinary amount of sugar in the blood is not exceeded, and so long as the organs which take up sugar from the blood and make use of it are not impaired in their activity. Putting aside all these conditions in which nothing more than a mellituria of brief duration occurs, there will still remain enough of the factors enumerated, which, however, cannot all be equally well set down to the account of diabetes. With no disposition to wholly ignore other possibilities, I may yet, in conclusion, specify the following as the most probable modes of development of diabetes, and as applying to the majority of cases: (1) *an abnormally heightened saccharinity of the chyle, or of the blood in the portal vein, or of the two together, in consequence of an impeded conversion of the sugar present in the intestine into lactic acid, or in consequence of accelerated absorption of the sugar*; (2) *an unnatural acceleration of the portal circulation, whereby, on the one hand, more sugar reaches the liver—a part of which, without being changed into glycogen, passes on into the circulation; and, on the other hand, the glycogen formed from sugar or other materials passes into sugar more rapidly and in greater quantity, and is washed away.*

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[1] Marburger Sitzungsber. der Ges. zur Beförd. der Naturwiss. 1866. No. 5.

Of course, the modes of development here set down do not exclude each other, and it is so much the more probable that they may, for the most part or altogether, occur simultaneously, since they do not act in opposition to each other. If, for example, a dilatation of the portal vessels and an acceleration of the intestino-hepatic circulation are present, the sugar will be more rapidly absorbed from the intestine, and also more quickly carried through the liver, and the result, an increase of the amount of sugar contained in the blood, will be all the more certain.

The nervous system may undoubtedly exert an influence upon the occurrence of these, as upon that of most of the causes of mellituria previously mentioned. Keeping in view only the modes of development last described, as apparently lying at the root of diabetes, it must be the nerve-tracts which govern the conditions of circulation, perhaps also of secretion, in the gastro-intestinal canal and the liver. In reality, indeed, those nerves whose injury certainly occasions mellituria contain vaso-motor (and secretory or trophic?) fibres for the organs mentioned, and we may explain the development of that mellituria which is occasioned by the nervous system by the intervention of vaso-motor disturbances. These nerve-tracts extend, as the above-quoted experiments teach (pp. 939–941), from the medulla oblongata, and perhaps also from still other points in the cerebrum and the cerebellum, through the upper part of the cervical spinal cord to the lowermost cervical and uppermost thoracic ganglion, and from thence through fibres of the sympathetic to the abdominal organs.

Now, in accordance with all this, we may conceive that diabetes is developed in a two-fold manner, either by the disturbances in the territory of the digestive canal and the liver, proceeding from any one point in these nerve-tracts, or by local causes immediately affecting those organs ; and, accordingly, we may establish various *forms* of the disease—*a diabetes proceeding primarily from the nervous system* (*neurogenic*), *and a diabetes proceeding primarily from the intestinal canal or the liver* (*gastro-enterogenic and hepatogenic*). If a diminished consumption of the sugar which reaches the general circulation takes place, which we left wholly in doubt, it should probably be included in the first (neurogenic) form.

Of course, it is easier to make such a division in theory than in practice ; but, if it is justified theoretically—and this seems to me to be the case, according, at any rate, to our present knowledge—then the practical problem comes up for solution, how far theoretical suppositions actually prove true. Theory shows practice the direction in which it must move in the study of diseases, and if at the present time the practical discrimination between such various forms of diabetes may have its great difficulties, it is nevertheless to be hoped that continued investigations, particularly with regard to the etiology and the development of the disease, as well as to its behavior under dietetic and pharmaceutical interference, may overcome these difficulties.

In the meantime we can even now positively designate a certain class of cases *as proceeding primarily from the nervous system.* These are the cases of diabetes which have appeared after traumatic or other injuries of the medulla oblongata, or in which post-mortem examination has revealed alterations in the territory of those nerve-tracts whose connection with mellituria has been proved. If these form thus far but a small minority of cases, be it remembered that in this respect we are dealing for the most part with very minute changes, recognizable only by careful microscopical examination, upon which, too, attention has only in recent times been bestowed; nay, that single nerve-regions, which, according to experimental researches in regard to etiology, may play a very important part (as, for instance, the ring of Vieussens, according to Cyon and Aladoff), have indeed never yet been investigated in diabetes mellitus. It must be further borne in mind that the nerve-centres governing the excretion of sugar may be irritated in a *reflex* manner from any part of the body whatever, without the necessity of any anatomical change being present in themselves, and that therefore there may be a "neurogenic" diabetes, the particular cause of which may lie far away from those nerve-tracts. Many of the cases which are developed in consequence of diseases of other nerve-parts than those mentioned, which are connected with mental affections, with epilepsy, and the like, should very likely be considered as neurogenic diabetes of reflex origin.

It is easily conceivable that, after the effect of experimental injuries of certain portions of the nervous system upon the development of mellituria had been proved, and after injuries and morbid alterations of the very same nerve-parts had been recognized as the immediate cause of diabetes mellitus, that is to say, after clinical experiences had been obtained which perfectly supplemented experimental researches, there was a tendency to look for the ultimate cause, even in other cases less clear in their development, in an affection of those nerve-parts; and surely not without warrant, since, as I have just now explained, even in many of these less clear cases, signs were to be found of an original or sympathetic affection of the nervous system of reflex origin. Whether, however, we are thereby warranted, thus early, as many authors do, in characterizing diabetes mellitus in *every* case, without exception, as a primary nervous disease, seems to me still questionable. There are cases enough of diabetes, in which at the beginning even the most careful observation and the most thorough examination of the patients disclose nothing which can be attributed to an affection of the nervous system, which for months and years show no nervous phenomena, in spite of pronounced diabetic symptoms, increase of thirst and of the quantity of urine, high saccharinity of the urine, etc. This is particularly common in well-nourished persons, accustomed to luxurious food, and somewhat advanced in years, in whom the disease has developed in an insidious manner; if in them phenomena occur in the subsequent course pointing perhaps to an involvement of the nervous system, such as general weakness, impotence, and a changing disposition, they may more correctly be attributed to the general disturbance of nutrition and the resulting cachexia, the disturbance of rest at night by the inclination to pass urine, and the like. To assume an *original* nervous affection in such cases would be more than venturesome. On the other hand, indeed, as has been mentioned, many facts point to the digestive organs as the point of departure and the peculiar seat of the disease. Less stress can be laid upon the fact that the occurrence of diabetes is sometimes observed immediately after dietetic errors or sudden changes of the accustomed condition in regard to food (see "Etiology"), since these cases are always but exceptions; but more upon the facts that the disease occurs with striking frequency in districts where the diet is chiefly vegetable—further, that, as has just been said, so frequently, apart from the abnormalities of the urinary secretion, phenomena pertaining to the digestive apparatus are alone observed for a long time—then, that injurious influences acting upon the digestive organs pre-eminently give rise to an aggravation—and finally, on the contrary, that favorable therapeutical effects are obtained by acting upon these organs, but not upon the nervous system; that, by means of that very agent which still always and rightly occupies the favorite position in the treatment of diabetes—the Carlsbad waters (or others like them), we can accomplish no direct effect in any way upon the nervous system, but merely a beneficial influence upon the digestive apparatus. We therefore believe that *the occurrence of a diabetes proceeding primarily from the digestive organs* must also be allowed. With the data at present available, however, we cannot admit a further division of this form into a "gastro-enterogenic" and a "hepatogenic," according as it proceeds from the digestive cavity proper or from the liver. It is probable, indeed, that the liver is involved in the severe cases, in which the excretion of sugar persists even upon the so-called exclusive meat diet. It would be more certain if this diet contained absolutely no sugar and no starch, but only other producers of glycogen (glycerine and gelatine). The liver, as well as the gastro-intestinal canal, may also be implicated in the lighter cases, in which sugar is voided only after the ingestion of starch and sugar in large quantities, and it is probable that both are often simultaneously involved (compare pp. 965–966). Thorough researches upon the excretion of sugar, under the administration of glycerine (fat) and gelatine might perhaps afford further information in particular cases.

We have still to discuss the *connection of the excretion of sugar with the other essential symptoms of diabetes*, particularly with the thirst and the increased secretion of urine. According to Vogel, "the serum of the blood, being highly concentrated by reason of its great saccharinity, takes up water by endosmosis with great avidity from all the parenchymatous fluids, as well as from the drinks and liquid food introduced into the stomach. The dryness of the mouth and throat thus occasioned explains the *thirst*, the *dryness of the skin*, *of the stools*, etc. In consequence of the absorption of the water the quantity of the blood is increased, the blood-pressure in the vascular system is heightened and gives rise to *polyuria*. Were no fresh ingestion of fluid to take place, the blood would constantly become more concentrated on account of the continued secretion of urine, and that, too, more markedly in a diabetic than in a healthy person, on account of its saccharinity, and it would keep on taking up water until its degree of concentration were brought to an equality with that of the parenchymatous fluids. When a healthy man drinks, the water which is absorbed into the blood speedily increases the quantity of the blood, and gives rise to diuresis. So soon as the greater part of the water taken up has been removed, the diuresis will stop. But let a diabetic drink, and the matter has to take on an entirely different aspect, even if in him the water drunk be as quickly absorbed from the stomach as in the healthy man. In the first place, the blood is diluted by the water which enters it; but the parenchymatous fluids being likewise rich in sugar, are much more concentrated in diabetics than in the healthy; they therefore divert a portion of the ingested water from the blood-serum, and consequently the diuresis soon after drinking will be less in such patients than in the healthy. In proportion, however, as the blood again becomes more concentrated by the secretion of urine, it in turn appropriates to itself the water which had been borrowed by the parenchymatous fluid, and thus the secretion of urine at a later period after drinking will be proportionately more abundant in diabetics than in the healthy." In this way, according to Vogel, is the fact to be explained that the water ingested is much less rapidly evacuated by the urine in diabetics than in the healthy, which Falck had attributed to a delayed absorption of the water (see pp. 895 and 954).

The latter part of this explanation, which deals with the retarded excretion of water in diabetics, seems weak *à priori*, since the equalization of the concentration of the blood and that of the parenchymatous fluids must take place in the healthy person also, and the difference lies in this alone, that the latter, on account of the lesser concentration of all his juices, does not need to absorb so much water into the blood as the diabetic does. Moreover, if we allow the diabetic to drink perfectly *ad libitum*, no greater concentration of his blood and of his juices at large can take place unless a greater excretion of water occurs through the kidneys. The fact also that the tardy excretion of the water drunk is observed in diabetes insipidus (which see) as well as in diabetes mellitus, makes against Vogel's explanation. But, on the other hand too, many considerations arise to indicate that, as this explanation demands, the saccharinity of the blood and juices, with their consequent concentration, is the sole cause of all the diabetic symptoms, and especially of the thirst and the increased secretion of urine, and that the quantity of sugar and that of urine must always go hand in hand with each other; for, in the first place, cases have been observed which began as diabetes insipidus, and in which the excretion of sugar did not take place until subsequently, as well as cases of diabetes mellitus, in which the sugar has disappeared for a long time from the urine, without the quantity of the latter returning to the normal standard (see p. 872). *Vice versâ*, a marked saccharinity of the urine has been observed with a normal or abnormally small amount of urine (diabetes decipiens), although, to be sure, for but brief periods—a few days. Kuelz (Beitr. II. p. 144) has shown, by comparative observations upon two female patients, that in spite of a like execretion of sugar in the urine, and of a like large ingestion of drink, the quantity of urine may for days together vary very much.[1]

Vogel's explanation, then, cannot apply to all cases, although it must be confessed that the excretion of sugar and that of water in the urine for the most part rise and fall together. But whether the thirst is occasioned by the abnormal saccharinity of the blood and the juices, and then the secretion of urine increased in consequence of the augmented absorption of water; or whether, on the contrary, the sugar does not, like chloride of sodium or urea, act as an irritant to the kidneys, goad them to an increased secretion of water, and thus cause the thirst—this indeed cannot be decided in individual cases. The diuretic effect of the sugar cannot by any means be wholly denied. But since augmented secretion of urine (and thirst) occur even independently of the saccharinity and not in direct ratio to it, it seems probable that in such cases, according to the experimental researches of Bernard and Eckhard, both symptoms, the increased diuresis and the excretion of sugar, are of nervous origin. Those investigators have ascertained that those points in the medulla oblongata, the irritation of which exerts the one or the other effect, lie very near each other. We may therefore readily conceive that the fundamental disease advances from the one to the other, and thus gives rise to a disproportion between the excretion of sugar and that of water.

Most of the other phenomena of diabetes mellitus can easily be explained by the loss of sugar and the strong determination of water to the kidneys, as has been stated in the proper place. The *debility* of diabetics must likewise be caused by the accumulation of sugar in the blood, for it disappears in proportion as the amount of sugar in the urine is diminished, and there is no reason to assume a primary profound affection of the muscles. Very likely, as Seegen supposes, an excess of lactic acid is formed in the muscles, thus occasioning lassitude. The tendency to *furuncles* and *gangrenous inflammations of the skin* is probably attributable to the irritation which the saccharine blood causes, and to the dryness of the tissues ; and lastly, the *emaciation* is the natural consequence of a great portion of the nutrient material remaining unemployed in the body.

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[1] The idea also that the *blood-pressure* is heightened, and consequently the amount of urine increased, by the absorption of the water drunk, is become untenable since *Worm Mueller* (Sitzungsber. der sächs. Ges. der Wiss. Math. phys. Klasse 1873. p. 573) has shown within how wide a range the vascular system is capable of accommodating itself to its contents without the lateral pressure within it being altered. But this is of secondary importance, since it is established by experience that the excretion of the water drunk devolves, as a rule, upon the kidneys.

Diagnosis.

The *detection of sugar* in the urine is the diagnostic sign of diabetes mellitus, without which there is no certainty, even if all the other symptoms are in the highest degree pronounced. As a rule, however, it is just these other symptoms that do and must lead the physician to test the urine for sugar. But it must be remembered that it is not always the *thirst and the more frequent desire to pass urine* which first attract the patient's attention, but that not infrequently *a general lassitude, furunculosis* and the *formation of carbuncles*, *itching of the skin*, *painful sensations*, *pains in the limbs*—considered as "rheumatism,"[1] but quite particularly *disturbances of vision*, first induce him to seek medical aid ; nay, that sometimes so trifling are the disorders present that they give rise to no complaint at all, and the sugar is rather found accidentally. It is, therefore, a rule to be well taken to heart, that testing the urine for sugar belongs to a complete examination of a patient—a rule which should never be disregarded in any diagnosis which is not established beyond all doubt.

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[1] A short time since a man presented himself to me at the polyclinic of the Augusta Hospital, whose complaint of weakness and pain in the legs, and other statements, pointed to an affection of the spinal cord and to an advancing arthritis deformans, of which the fingers already showed traces, until an examination of the urine, undertaken on account of uncertainty of the diagnosis, showed a very considerable amount of sugar.

On the other hand, as has already been stated (p. 964), there are conditions of a physiological or pathological nature, in which sugar appears in the urine, without there being any question of an actual diabetes mellitus. Under these circumstances the saccharinity of the urine does not, to be sure, reach that high grade which it usually has in diabetes ; but yet no satisfactory distinctive sign can be found in that, because there is no standard limit to the saccharinity, below which it can be assumed that we are dealing with but a transient glycosuria, and above which diabetes begins. Well-marked symptoms of the latter have been observed with a saccharinity of 0.5, nay, even of 0.3 per cent. (Abeles), and, on the other hand, in pregnant and nursing women, who showed no other symptoms whatever attributable to diabetes, nearly two per cent. of sugar has been found in the urine (see p. 960). In accordance with experience thus far, it can only be said, that *a saccharinity of over two per cent. certainly occurs only in diabetes, but that a lower saccharinity does not exclude diabetes.* In the latter case the other diabetic symptoms must serve as aids in the diagnosis, and further, the circumstance that non-diabetic mellituria is temporary, like the conditions which give rise to it, and which, therefore, are likewise to be taken into consideration.

As concerns the *recognition of sugar in the urine*, we may indeed conclude with some probability that sugar is present from certain external peculiarities—its pale, greenish-yellow appearance, the peculiar smell, and especially its high specific gravity, and, in case of need, we may have recourse to the taste ; but its positive detection can only be accomplished by chemical methods.

Such methods have been described in great number, but in practice many of them are superfluous, and some of them are useless on account of their minuteness. Most of them are founded upon the property of sugar to reduce oxides in alkaline solution, and amongst these Trommer's test, to be described presently, deserves to be ranked foremost on account of its certainty and its ready applicability. If the urine be free from albumen, it is sufficient, as a rule, without further preparation, to make it strongly alkaline by the addition of liquor potassæ or liquor sodæ (about one-quarter of its volume) in a small test-tube, and to add to it drop by drop a tolerably concentrated (1:5) solution of sulphate of copper. If the urine contain sugar (that is to say, more than the mere traces which do not come into consideration), more or less of the sulphate of copper is resolved, on shaking, into a clear blue fluid. We should avoid adding more than will dissolve. The upper part of the liquid should now be carefully heated nearly to boiling, until a yellowish red cloudiness is noticeable here, which soon pervades the whole urine, and, according to the amount of sugar present, forms more or less of a deposit of precipitated suboxide of copper. *The reaction follows the course described, i. e., with the evident deposition of a precipitate of a color between yellow and red, only if sugar be present;* and, indeed, according to Seegen, it is still characteristic with as little as 0.3 per cent.

With smaller amounts of sugar, *and also, under certain circumstances, with a larger amount*, the precipitation of suboxide or hydrated suboxide fails to take place; the oxide of copper is reduced, to be sure, and the liquid is colored green at first, and then brownish or a dusky golden yellow, but the suboxide (and hydrated suboxide) of copper remain in solution, partly on account of their minute quantity, and partly on account of the presence of certain substances which increase their solubility, such as creatinine (Kuehne and Maly[1]), ammonia, etc. This coloration of the urine, without the precipitation of suboxide of copper, is not a proof of the presence of sugar, for it is also produced by other reductive constituents of the urine, by uric acid and the coloring matter of urine. In such doubtful cases we shall still generally succeed in obtaining an undoubted result, namely, an evident precipitation of suboxide of copper, by diluting the urine, especially if it be somewhat concentrated, before applying Trommer's test. But, if not, it is judicious, according to Seegen, to filter the urine through animal charcoal one or more times until it is completely decolorized, to wash the charcoal with a little water, and to subject this water to Trommer's test, which then, provided the urine originally contained 0.05 per cent. of sugar, causes a precipitate of suboxide of copper. During the washing the charcoal retains the substances which interfere with the precipitation of the suboxide of copper, as well as the other reductive admixtures (uric acid), and the test consequently becomes at once very sensitive and conclusive.

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[1] Wiener acad. Sitzungsberichte. 1871. LXIII. p. 477.

No other methods of detection yet described offer any superiority, and they are inferior in sensitiveness to Trommer's test, especially when the latter is applied with the modification last described.[1] They may serve to confirm this test, but they cannot replace it in doubtful cases. On account of its ready applicability, we must particularly mention Heller's or Moore's test, which consists in heating to the boiling-point the upper portion of a quantity of urine mixed with liquor potassæ in a test-tube. If sugar be present, this portion continually becomes darker colored until it is of a deep brown, and thus contrasts markedly with the lower, clear part of the liquid. If, however, the amount of sugar be small, the difference of color is difficult to recognize, and, moreover, a browning of the urine is occasioned by others of its constituents. If we neutralize the urine thus boiled with nitric acid, we shall notice an evident smell of caramel, if the amount of sugar be not too small.

It is of great importance, where diabetes is suspected, and a single examination of the urine has not yielded a positive result, to examine the urine repeatedly, and *especially several hours after eating*. To be quite certain, it is well to let the patient eat of food abounding in sugar and starch, and then to examine the urine passed some hours afterwards. If, after one or more such periods, it is free from sugar, diabetes may be excluded.

For the *quantitative* estimation of sugar, it is best to use the

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[1] Upon this point I would refer to the manuals and text-books of medical chemistry, to *Neubauer* and *Vogel's* Anleitung zur Harnuntersuchung, etc. A test given by Almén (see Prager Vierteljahrschr. 1869. CI. p. 19 of the bibliographical index) may perhaps yet prove of advantage. According to him, two parts of tartrate of soda and potassa are to be heated with forty-eight parts of liquor potassæ (of a specific gravity of 1.33), and one part of subnitrate of bismuth dissolved in it. The urine should be boiled for a few minutes with about one-tenth its bulk of this test-liquid, and will throw down a black precipitate with even one-fortieth of one per cent. of sugar. Uric acid, creatinine, and ammonia do not seem to interfere with this test.

titration method of Fehling (by means of an alkaline solution of tartrate of soda and potassa, to which a sufficient, definite quantity of sulphate of copper is added), or that of Knapp (by means of an alkaline solution of cyanide of mercury of known strength). Both methods require but little skill in their application, and give positive results which correspond well with each other. Full information concerning them and the precautions which Fehling's method, especially, demands in its employment, will be found in the text-books of medical chemistry.

Somewhat more convenient, but also less satisfactory, is the examination by means of Soleil-Ventzke's or Mitscherlich's polarization apparatus, which is founded upon the property of grape-sugar of turning the ray of polarized light to the right. This method, as a rule, gives the proportion of sugar too low, even upwards of one per cent. too low. Very dark-colored urine should first be decolorized, preferably by a small amount of solution of acetate of lead accurately measured, for otherwise it is not sufficiently transparent.

The *fermentation test* has also been used for the quantitative estimation of sugar. It is founded upon a determination of the loss of weight which a solution of sugar undergoes by the escape of the carbonic acid formed on fermentation. Its results are no more accurate, but its execution far more inconvenient, than those of the titration methods. However, if chemical apparatus be wanting, fermentation may be employed for the quantitative estimation by the very simple and pre-eminently available methods proposed by Roberts[1] and Manasseïn,[2] which, as it seems, give very good results—sufficient, at all events, for the requirements of practice. The specific gravity of the urine being taken with a trustworthy urometer before and after fermentation, which is produced with well-washed yeast, the difference is multiplied by 1,000, and the product divided by 4.56.

In conclusion, it should be remembered that urine *containing albumen* should be freed of albumen before *any* test for sugar is applied, and this is best done with acids and boiling.

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[1] Edinb. Med. Journal. VII. 1862. p. 326.

[2] Deutsches Arch. f. klin. Med. X. 1872. p. 73.

Course, Duration, and Results.—Complications.

With very few exceptions, the *course* of diabetes is *chronic*, and, unless complications and the final phenomena occasion the contrary, *free from fever;* but it behaves differently, according to the greater or less capacity of the body to retain and make use of sugar and sugar-producers, *i. e.*, according to the influence which a restricted ingestion of hydrocarbons with the food exerts upon the excretion of sugar in the urine. Those more benign cases, in which an exclusively, or even but chiefly animal diet causes the sugar to disappear (the "light form," the "first stage"), not only progress more slowly in general, so long as this influence is present, but also involve far fewer disturbances than the others, in which the exclusion of vegetable food is capable, to be sure, of diminishing the sugar in the urine, but not of wholly removing it (the "severe form," or the "second stage"). With proper management, patients of the former sort may for a long time find themselves tolerably or entirely well. With the disappearance of the sugar the thirst also disappears, and the increased secretion of urine, the emaciation, and the muscular weakness, and even cataracts, recede, so that for a time such patients give one the impression of their being perfectly healthy. Not infrequently they even acquire, for a longer or shorter period, the capability of taking with impunity hydrocarbons in quantities which formerly gave rise to the excretion of sugar. That is to say, the morbid process has come to a *stand-still*, or has even undergone *diminution.* It is important to know of this behavior, upon which, besides diet, still other circumstances, such as climate, season of the year, mental disposition, and the like, have an influence, in order that we may not hastily ascribe the favorable changes in the patient's condition to a drug, as has happened often enough.

How long the disease may possibly be kept in abeyance in patients of this sort, we can by no means say, although it is conceivable theoretically that, by avoiding all injurious influences, the occurrence of mellituria and the other symptoms connected with it may be restrained for an unlimited length of time, and even until life be ended by other causes. These patients are like the subjects of the hemorrhagic diathesis, who show no outward signs of disease and are free from danger, so long as they escape all injury. But, as most hæmophiliacs die prematurely of their disease—because it is impossible to avoid all, even the slightest, causes of hemorrhage—so finally these diabetics succumb to their disease, because it had merely slumbered for a period of greater or less duration, but was not eradicated. Be it that they overstep, intentionally or unintentionally, the bounds within which they are able to assimilate sugar and its formatives, which in the course of time becomes utterly unavoidable; or that the faculty of assimilation gradually diminishes—it is impossible to keep patients permanently on a diet upon which they no longer void sugar, and from this time onward they follow the same course with those patients in whom diet was never able to make the sugar wholly disappear from the urine.

In the latter the course is less restrained from the beginning. At first, indeed, variations occur in the amount of sugar excreted and consequently in the general health; but true pauses, with perfect subsidence of all disorders, do not take place at all, or are of but quite brief duration. In these patients all the diabetic symptoms—thirst and polyuria, hunger, emaciation, weakness, etc.—reach the highest grade. They constantly grow weaker, and finally yield to some slight ailment or another—an accidental intercurrent disease, or to one of the ordinary complications, such as pulmonary consumption, a carbuncle, gangrene, etc.

The *period of life* has a decided influence upon the course of the disease. The younger the patients are, the more malignant and the more rapid, in general, is the course. In persons of advanced years the disease makes its appearance for the most part much more mildly; whilst in the aged we not infrequently observe an excretion of sugar, now more, now less in quantity, for a long time, and also an increased secretion of urine, with but quite trifling additional symptoms, and without those profound disturbances of nutrition which so speedily make themselves noticeable in young persons.

Since the time of Th. Willis,[1] who tells of a woman who every morning passed an amount of urine far exceeding what she had drunk, many authors have spoken of an *intermittent diabetes.* In so far as this relates to true diabetes, and not, as may perhaps have been the case with the older authors, to a temporarily increased secretion of urine from other causes, most of the cases so designated are those in which sugar appeared in the urine in connection with malarial diseases, and in a periodical manner, with or without a typical attack of fever; or they are ordinary cases of diabetes mellitus, benign as a rule, in which, as so often happens, the sugar disappeared from the urine at times and in a quite atypical manner, and reappeared upon any provocation whatever. Those typical excretions of sugar appearing with intermittent fever, which Burdel, in particular, says that he has observed in great number (see also Seegen, Monogr. p. 44), do not, moreover, follow the course of diabetes mellitus, but exemplify the transitory forms of glycosuria, concerning the possible causes of which mention has already been made (p. 963). It is self-evident that they are not to be placed in the same rank with cases of true diabetes, which have occasionally been seen to make their appearance after long-continued and obstinate intermittent fevers, as well as after many other debilitating diseases (see "Etiology").

Quite unique is the case related by Bennewitz,[2] of a woman who, in the twentieth year of her age, and while pregnant, became affected with diabetic symptoms, which suddenly disappeared after parturition, returned again in greater severity in the following year, during her fifth pregnancy, and again disappeared after confinement, and finally recurred for the last time during her sixth pregnancy, six months later, but now with much less severity, after which her health was not again disturbed.

The usual *duration* of diabetes extends over several years. The time cannot be quite precisely stated, for the disease is scarcely ever discovered until it has already reached a certain height. From a hundred cases Griesinger constructed the following table of durations:

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[1] See *Salomon*, l. c., p. 518.

[2] Hufeland's Journal. LXI. 1865. p. 114.

Less than ¼ year	1
From ¼ to ½ "	2
" ½ " 1 "	13
" 1 " 2 years	39
" 2 " 3 "	20
" 3 " 4 "	7
" 4 " 5 "	2
" 5 " 6 "	1
" 6 " 7 "	2
" 7 " 8 "	1
Not specified	12
	100

According to this, three-quarters of the diabetics die after the disease has lasted from six months to three years. Dickinson's collection of 25 diabetics who died in Guy's Hospital leads to the same result, for 21 of them were shown to have suffered from the disease from six months to three years. These statistics are impaired in value, however, in that they refer exclusively or preponderatingly to hospital patients, who have lived with their disease for a length of time under unfavorable conditions—conditions which, as experience shows, materially accelerate its course. Statistics which should also take account of patients from the well-to-do classes would most decidedly give more than from six months to three years as the medium duration of diabetes, for the number is not small of diabetics who live longer, and who frequent the bathing establishments from five to six years, and longer yet. It is certain that, under appropriate treatment, the disease may last still longer, although a duration of over ten years must always belong among the exceptions. There is no lack of individual examples of the sort. Bence Jones tells of a clergyman who was still in good health, although Prout had detected sugar in his urine sixteen years before; Dickinson, of an innkeeper, in whom marked symptoms of the disease had been present fifteen years before, and who, while in tolerable health, was voiding 100 grammes of sugar daily; and Lebert,[1] of a Deputy of the Paris Constituent Assembly of 1848, who had suffered with diabetes for eighteen years, was in good health when on appropriate diet, but immediately, upon any neglect of this, again passed sugar in his urine. In strong contrast to these are the cases, rare though they be, of extraordinarily brief duration—those in which, from the apparent beginning of the disease until death, but a few weeks or even days elapse, and which have hence been designated as "*diabetes acutus*" or "*acutissimus*." It is very probable that in such cases, which, for that matter, occur, almost without exception, in children or young persons, the excretion of sugar, and perhaps the other derangements too, have existed for a long time unobserved, until a sudden change in the patient's health arrested attention, so that in these cases, as in most others, an accurate specification of the time cannot be made. In the case observed by Wallach, the duration of the disease, from its first beginning until death, was ascertained positively to be five weeks. Other cases running a fatal course within a few weeks have been contributed by Dobson, Roberts, Beckler, W. F. Smith, and myself. In a case by Becquerel, the disease, in a boy nine years old, would seem to have lasted but six days.

The usual *result* is *death*. It either happens gradually, by complete exhaustion, in which case death is not uncommonly preceded for a long time by dropsical symptoms, œdema of the lower extremities in consequence of the watery condition of the blood; or it occurs in the course of a few days, with cerebral symptoms, which give the impression of a blood-poisoning, and are known as "diabetic coma" (see p. 916), but which are occasionally induced by an effusion of blood into the brain. A very large number of diabetics die of pulmonary consumption, a small number of complicating local diseases which of themselves are not necessarily fatal, but which prove destructive in consequence of the slight resisting power, the "lability" of their tissues. The termination in perfect *recovery* is entirely discredited by many physicians; and certainly, if it ever occurs, it is exceedingly rare, for a pause in the disease—an improvement continuing for a longer or shorter time, which, as has been mentioned, is not at all infrequently observed—must not be taken for perfect recovery. To these very rare exceptions belongs a termination of diabetes mellitus in diabetes insipidus, with consecutive recovery, as Plagge observed it.[1]

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[1] L. c., p. 656.

The most usual *complications* of diabetes have already been spoken of (see "Pathological Anatomy" and "Special Symptomatology"). In addition to these, I once observed a complication with arthritis deformans of the finger-joints. (See p. 972, note.)

Griesinger adduces as remarkable the *rarity* of *cancers*, *diseases of the heart*, and *rheumatic polyarthritis*, in diabetics. Amongst 225 cases compared statistically, and amongst a large number otherwise made use of, he found not a single undoubted case of cancer, only three in which the data allowed of disease of the heart or the vessels being inferred (in one of which the diabetes, relapsing several times and again intermitting for years together, seemed to form a mere episode in the course of a heart disease; compare above, p. 963), and only one or two of "acute rheumatism."

Prognosis.

Since, in accordance with experience thus far, a permanent and complete recovery does not take place, the prognosis as regards the final result of diabetes is unfavorable. As regards its course, it is dependent to the greatest extent upon the *influence of the diet* upon the excretion of sugar, concerning which repeated mention has been made in the foregoing. The more decided is this influence—*i. e.*, the smaller the quantity of sugar becomes on restricting the hydrocarbons (the so-called meat diet being used)—then so much the more favorable is the case in general. However, to form a correct judgment, we must keep the patient on the stringent diet for several days before examining the urine, for the influence of any preceding diet may make itself felt for some time. *Age* is next in importance, for the younger the patient is at the beginning of his disease the more rapidly will it progress to the fatal end. A great deal depends upon whether the *external conditions*, the occupation and habits, the peculiarities of his character, place the patient in a position to lead an appropriate course of life and adhere to the prescribed diet. Not every patient is so situated as to be able to eat nothing but expensive animal food, and not every one who is so circumstanced is sufficiently master of himself to assuage his hunger with that alone, in opposition to his habits and inclinations. Patients who live under favorable external conditions, and conscientiously accept the physician's prescriptions, may remain for a long time unmolested by the disease. Finally, the *condition of the digestive organs* comes up for consideration. So long as they digest the necessary quantity of animal food, the disturbances of nutrition may be kept within bounds. Should any abhorrence towards this food occur, and digestive derangements be thus occasioned, the prospect becomes darkened, for this is the rock upon which all diabetics who are not sooner carried off by some complications are wrecked at last.

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[1] Ein Fall von Diabetes traumaticus. Virchow's Archiv. XIII. p. 93.

All complications aggravate the prognosis, most especially gangrenous processes and pulmonary consumption.

Treatment.

No special advice can be given for the *prevention* of diabetes.

The *treatment* itself, so long as the precise causes of the disease are not certainly known, has to keep in view for its prime object the reduction of the amount of sugar in the blood, since most of the disturbances, and the most dangerous of them, are attributable to the abnormal saccharinity of the blood. Probably this will be disputed by no one at the present time ; and hence, scarcely any one will now speak in favor of feeding with sugar in diabetes, which Piorry [1] advised with a view to replace the lost sugar, or with sugar-forming substances, as Schiff proposed, in order to satisfy thus the demands of the sugar-forming ferment, and so limit the formation of sugar from the constituents of the body. Moreover, medical experience has indisputably demonstrated the harm of feeding with sugar, and has shown that the diabetic cannot, like the healthy man, make use of the grape-sugar taken in with the food or developed within the body. *On the contrary, therefore, the withdrawal of grape-sugar, and of such substances as are converted into grape-sugar on their way into the blood, is to be obtained at any price.* Could we wholly and forever abstract sugar and its formatives from the diabetic's food, without doing injury to his nutrition, we should not, indeed, cure his disease, but we could make it entirely harmless. We can nearly attain this by replacing vegetable with *animal food*, which is infinitely poorer in hydrocarbons. What can be accomplished by this is well enough known, and has repeatedly been mentioned in the preceding pages. Only one difficulty, but that a very palpable one in practice, opposes its unqualified and exclusive employment: that is, the repugnance which is soon manifested against the uniform diet, and the digestive derangements which are occasioned by the large quantities of meat necessary to meet the demands of nutrition. It may here be mentioned incidentally that Lauder Brunton proposes to feed diabetics preferably with *raw meat*, in order that they may ingest a larger quantity of the sugar-destroying ferment contained in the muscles. With a like view, *yeast* was formerly recommended, but was given up as ineffectual.

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[1] Comptes rendus. XLIV. 1847. p. 133.

But it is not all hydrocarbons, nor even all sorts of sugar in the strict sense of the term, that exert the same effect upon the excretion of sugar. It was known, indeed, to the older observers, such as Babington[1] and Barlow,[2] that by no means all vegetables increased the amount of sugar in the urine of diabetics; that, in particular, green vegetables, such as cabbage, spinach, certain beets, and the like, could often be eaten without injury. Investigations in recent years have not only fully established these facts, but have also furnished the explanation of them in the different amounts of one or another hydrocarbon contained in the vegetables, and in the unequal use made of them by diabetics. It has already been mentioned (p. 953) that, according to Kuelz, *mannite*, *inuline*, *levulose*, and *inosite* are perfectly assimilated, even by those diabetics who still excrete sugar, even when on animal diet—*i. e.*, they are used up in the body in some way; that *sugar of milk* sometimes behaves in this way, and at other times not; furthermore, that *glycerine* likewise may be taken in certain cases without increasing the excretion of sugar, and that, too, by patients who continue to void sugar on a meat diet. It has also been previously and repeatedly hinted how these facts might be turned to account in the further study of diabetes and of its various modes of development, with some prospect of a result. Even now they are of the utmost significance in regard to the treatment, since on the strength of them we are enabled to effect a variety in the diabetic's bill of fare, and thus essentially facilitate his conforming to the prescribed diet.

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[1] *R. Willis*, Urinary Diseases and their Treatment. London, 1838.

[2] Guy's Hospital Reports. V. p. 282.

In strict accordance with the foregoing, we can designate, besides salts, extractive matters, and water, only *albumen* and *mannite* as nutritive substances which are *allowable for diabetics under all circumstances*, since it is proved that glycogen and grape-sugar are not formed from them at all, or only in extremely small amount; perhaps also *inosite*, the influence of which upon the formation of glycogen has, however, not yet been investigated, but which, as has been mentioned, seems to be assimilated by all diabetics. As *conditionally allowable*, we must specify *glycerine* (*fats*), *sugar of milk* (and *galactose?*), *inuline*, and *levulose*, all of which, to be sure, are generators of glycogen, and therefore of sugar, but are capable of assimilation by diabetics to a greater or less extent, differing perhaps according to the different forms of diabetes or according to individual conditions. In what cases they are assimilated, and in what ones they are not, we cannot now specify, and probably this will never be settled except by experiment. From a theoretical standpoint, they must be rejected in all those cases in which, on account of changes in the liver, glycogen is changed into sugar more rapidly than normal (see p. 956). The same is true of *gelatine*, concerning the action of which upon diabetics methodical investigations are, however, still wanting.[1]

From this one can judge approximately what articles of diet are likely to be borne well by patients suffering from diabetes, and what they should either avoid altogether, as being decidedly injurious, or take only at times and with caution, on account of their more or less injurious effects. As a general thing, animal food contains the beneficial and the more or less harmful elements combined in the proportions most favorable for the diabetic. Most to be recommended, therefore, are the flesh of mammalia, birds, shell-fish (oysters, mussels, crabs, etc.), and fishes; then cheese (and poor rather than rich cheese), and eggs —of which, however, the white is more to be recommended than the yolk. Of vegetables, we may mention: the greens which are used as salad, cucumbers, water-cresses, spinach, asparagus, the various kinds of cabbage, oyster-plant, radishes, together with yellow beets and truffles. The fatty articles, butter, lard, and oil, are not unconditionally admissible, on account of their containing glycerine, although this is of small amount in comparison with the fatty acids, and glycerine does not, of itself, always increase the excretion of sugar in the urine; but they cannot be stricken from the list of articles allowed, chiefly because the fats can scarcely be dispensed with from the food, even for a short time. Moreover, as a rule, diabetics bear fats very well, and many of them, indeed, according to my experience, have a great predilection for them. (Compare what was said under the head of fatty acids and glycerine.)

Grape-sugar, cane-sugar, honey,[2] flour, and all highly farinaceous articles, particularly bread, potatoes, pulse, rice, groats, sago, Indian corn, chestnuts, and the like, should be avoided as far as possible. Fruits need not be so universally and decidedly eschewed, as is now generally done, for many of them contain more levulose than grape-sugar. The acid fruits, in particular, such as sour cherries, strawberries, and currants, need occasion least hesitation. Nuts and almonds contain but little of the hydrocarbons, but chiefly fat, and are therefore admissible too.

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[1] In the case observed by *Blumenthal* (l. c.), gelatine in large quantities was taken, together with the meat-diet, for a length of time, as I have been informed by oral communication, but without any effect upon the excretion of sugar.

[2] According to *Wadham*, honey does not increase the excretion of sugar. This may perhaps be the case with many patients, as honey consists in great part of levulose.

It is self-evident that in the preparation of the food, injurious ingredients are to be avoided, such as flour, grape-sugar, and cane-sugar. Perhaps in this respect common sugar might be advantageously replaced with mannite, as proposed by Kuelz.

It is hardest for the patients to do without *bread*, and yet it is for them one of the most injurious articles of food, on account of its containing a great deal of starch (over 80 per cent. of the solid constituents). The effort has often been made, therefore, to replace it with other pastry containing little or no starch. Thus, in 1841 Bouchardat invented *gluten-bread*, made from flour which has been, or is said to be, deprived of its starch by washing with hot water. But, in general, such bread, wholly free from starch, is impracticable, for no dough can be made without starch; and moreover, by the washing, the flour is deprived of a great part of its salts, and, partly on this account probably, is rather insipid. Moreover, the various kinds of gluten-bread in the market differ very much in the amounts of hydrocarbons which they contain; according to Budde, the smallest amount (two per cent.) is contained in the gluten-bread prepared at the factory of Rasmussen and Heegard, of Copenhagen.[1] Another process for freeing bread from starch and sugar was tried by Vogel, on the advice of Liebig, and found worthy of recommendation. By that method, thin slices of bread are treated with an infusion of malt, which, by means of its diastase, converts the starch into sugar and dissolves it; they are then washed, dried, and slightly toasted. Prout and Camplin have recommended bread made from washed bran-flour, but this has no advantages over the gluten-bread, but, indeed, the disadvantage of being more difficult of digestion and still more unpalatable. About the same is true of the pastry prepared from washed potatoes, after the method of Palmer.[2] Pavy has had an *almond-bread* made, containing eggs and almonds freed by hot water of their small contingent of hydrocarbons.[1] When well prepared it is taken by many patients not unwillingly, but it is more difficult of digestion and immeasurably dearer than common bread. Finally, Kuelz (Beitr. I. p. 145) has had biscuits made of *inuline*—which, as has been mentioned, he found to have no effect, in small quantities at least, upon the excretion of sugar—together with milk, eggs, and salt. He reminds us that in many districts a bread is prepared—the *lichen-* or *moss-bread*—of Iceland moss, the chief constituent of which is moss-starch (lichenine), a variety of inuline. Perhaps this will be used by diabetics in the future, on account of its cheapness and nutritive quality, and furnish them with an available substitute for common bread, which is not fully accomplished by any of the other substitutes mentioned, even the best of them, Pavy's almond-bread. Until then they can never be wholly deprived of ordinary bread, but must be allowed more or less of it daily, at least at times, according to the severity of the case. Kuelz advises that patients should take their allowance of bread within a short time, or all at once, instead of dividing it among several meals, because in the latter case the sugar formed from the bread circulates longer in the blood, and occasions injurious effects, whilst the larger quantity reaching the blood at one time is quickly excreted, and therefore has less time to do harm. This idea does not seem to me correct; on the contrary, we may rather expect that, with a more gradual accession of smaller quantities of bread (and sugar), they will be converted in the intestine or otherwise used up in the body, without increasing the saccharinity of the blood; whereas, if larger quantities be taken at one time, a portion will certainly escape conversion, just as, but in greater degree than, a single excessive ingestion of sugar may give rise to mellituria in the healthy.

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[1] See *Seegen*, Monogr. p. 167.

[2] Bull. gén. de thérap. 1849. 15 Mai.

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[1] *Seegen* recommends the following preparation: Beat a quarter of a pound of blanched sweet almonds in a stone mortar for about three-quarters of an hour—as fine as possible; put the flour thus produced into a linen bag, which is then immersed for a quarter of an hour in boiling water acidulated with a few drops of vinegar. The mass is then intimately mixed with three ounces of butter and two eggs, the yolks of three eggs and a little salt are added, and the whole is to be stirred briskly for a long time. A fine froth is to be made by beating the white of the three eggs, and added. The whole paste is now put into a form smeared with melted butter, and baked with a gentle fire.

In choosing drinks, we must be guided chiefly by the amount of *sugar* (and other hydrocarbons); the more they contain of them the more injurious are they, as a matter of course. It is self-evident that there need be no hesitation about drinking plain water, seltzer-water, soda-water, or acidulous drinks. Coffee and tea contain sugar and its producers, to be sure, but in such small amount that they may be allowed, especially in weak infusion, and likewise infusion of cacao-shells, whilst the cacao-bean (chocolate) should be wholly avoided. Many patients miss sugar the most from the drinks which they are in the habit of sweetening, such as coffee, tea, etc. Of late years I have furnished them with a very welcome substitute in glycerine, which was previously recommended for this purpose by Beale[1] and Garrod.[2] At present, from the researches of Luchsinger, Salomon, and Kuelz (see p. 935), I would give mannite the unqualified preference.

Milk, notwithstanding its containing some four per cent. of sugar, is not to be absolutely withheld, for sugar of milk commonly has no effect upon the excretion of sugar, and the same is true of *whey* and *buttermilk*. In regard to *cream*, we may say about the same as of the fats. Donkin highly commends the systematic and exclusive use of *skimmed milk*, whilst others, as Barclay,[3] Pavy, Roberts, and Dickinson, have seen nothing but detriment from it. I myself attempted this treatment in one case, but as early as the third day the patient refused to continue it, although other food was not absolutely forbidden him, as Donkin requires; and indeed, it is difficult to see how any one should be able to live for weeks upon nothing but skimmed milk, deprived as it is of a great part of its fat and albumen.

Opinions have been, and are still, divided as to the admissibility of *alcohol* and the alcoholic drinks. Many, such as Camplin, Rosenstein, Guenzler (Griesinger), and others, have seen the excretion of sugar increased after drinking wine, whilst other physicians of great experience, like Bouchardat, Prout, Pavy, and Seegen, have observed no increase, even upon very free wine-drinking. Recently, in a case very thoroughly observed, Kuelz found no increase in the excretion of sugar during the use of wine and spirit, and has allowed wine to be taken in other cases also without injury. I myself, too, have never seen any harm from the moderate use of spirituous drinks by patients who are accustomed to them. In persons unaccustomed to them, their use may be injurious perhaps under certain circumstances, but such patients can dispense with them entirely, except under specially urgent circumstances, such as prostration and the like. The sweet wines, champagne, and cider, should be entirely avoided, and of the others, preference is given to the red wines on account of their slightly astringent effect. Sugared brandies (liqueurs) should also be avoided, and beer, too, as much as possible. *Koumys*, however, is well worthy of trial, especially if old and free from sugar.

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[1] Union Méd. 1864. No. 12.

[2] Med Times and Gaz. 1864. Jan.

[3] The Lancet. 1873. I. No. 21.

Notwithstanding the tormenting thirst and the dryness of the mouth, it is not advisable to let patients drink unrestrainedly, lest the frequent desire to pass urine be further increased. It is better to let them take pieces of ice into the mouth, and keep them there as long as possible ; but we should avoid acids, although they are craved for allaying thirst, on account of their injurious effect upon the teeth, which in diabetics show a tendency, apart from this, to decay.

The foregoing may serve as a guide for regulating the diet of diabetics in general, without giving them a loathing for their food. We should not follow a fixed rule, and prescribe the same bill of fare for all diabetics, nor even keep the same patient upon the same diet at all times, and least of all should we insist upon a perfect exclusion of all vegetable food. Even if the patient's circumstances and his strength of will admitted of such an extreme limitation in his choice of food, it would soon be opposed by the condition of the digestive organs. It cannot, therefore, be often enough repeated, that we must take into account individual conditions and the peculiarities of every single case, which, of course, often can only be learned by long observation. A diabetic who is excreting a moderate quantity of sugar, but is able to make good the loss by eating and drinking, is better off than one from whose urine the sugar disappears by reason of inanition and at the expense of his nutrition.

Particular regard should be had to the *care of the skin* in diabetics. Warm baths are very serviceable to them, to combat the dryness of the skin and the tendency to eruptions, furuncles, etc. According to circumstances, too, different additions may judiciously be made to the baths, or sea-bathing may be employed for invigorating the patient, subduing nervous derangements, and the like. Protection against catching cold, by means of warm clothing, is to be stringently recommended to patients, on account of their diminished power of resistance and the constantly threatening danger of pulmonary consumption. Whoever is in a position to do so, will do well to select a mild climate for a prolonged residence.

According to the observations of Bouchardat and Trousseau, and more especially of Kuelz, active *muscular movements* are capable of considerably lowering the excretion of sugar, and Trousseau even thinks "that exercise cannot be highly enough recommended to patients, and that, with a wholesome but not too stringent diet, and daily bodily exercise (long walks and hunting), diabetes, especially in fat people, may rather be called a disability than a severe disease." It is certain that bodily exercise is beneficial to the general health of well-nourished or even quite corpulent patients, especially if they move about much in the open air. But in this matter we must guard against extremes in either direction, and all the more since it is just after bodily toil, forced marches, and the like, that a sudden aggravation of the morbid condition has not infrequently been observed (p. 932). In patients already reduced we should therefore be very careful in advising exercise.

Regulation of the diet must be the chief feature of any treatment of diabetes; it can never be replaced by drugs, but often enables us to dispense with the latter. Upon this point all physicians have been completely agreed since Rollo's recommendation, and more particularly since Bouchardat's labors in establishing an appropriate diet. Nevertheless, *drugs* have been sought for, since then as well as before, which should either support and perfect the effect of diet, or repress the chief symptoms even without stringent diet, or indeed do away with the disease altogether. It is impossible to enumerate all the means which have been proposed with one or another of these views, for we may say without exaggeration, that there is scarcely any agent among the great store of drugs of all periods and all countries which has not at one time or another been employed against diabetes, and from which a result has not been recorded, even if only at the hands of its commenders and propagandists. Whatever changes there have been in the views held upon diabetes in the course of centuries, however many of them have fallen into oblivion—each one has left its traces in therapeutics. Every new theory has called forth new indications for treatment, and has striven to meet them in the spirit of its period and with the means and methods at its command. So long as opinion was governed by Galen's doctrine of a deranged action of the kidneys, *astringent* agents and methods—those which *diminished secretion*, *derivatives*, and *sudorifics*, or, finally, agents to which a *specific action on the kidneys* was ascribed, were recommended in turn. Those of the latter category —medicines which irritate the kidneys—are now almost given up as injurious, only one of them—*juniper berries*—having retained a certain repute even up to the most recent period, and being recommended now and then.

Subsequently, as the fundamental error in diabetes was looked for in the digestive organs, these were taken as points of attack in the treatment, and *emetics* and *cathartics* were employed, according as an improvement of the function of the stomach and intestinal canal, or of that of the liver, was kept in view; or medicines were given which arrested *abnormal transformations and fermentations*, such as creasote and carbolic acid, or which seemed to take the place of *deficient digestive* juices, such as rennet, ox-gall, acids, and alkalies. Next in order came the agents which seemed to promote the *combustion of the sugar*, such as oxygen and ozone, peroxide of hydrogen, permanganate of potassa, chlorine, and alkalies; and these again were supplanted by drugs which promised an effect upon the *nervous system* or upon the circulation in the liver, such as narcotics, strychnine, quinine, and ergot. In addition, agents were proposed *to take the place of sugar or its normal products of metamorphosis in the organism*, such as alcohol, lactic acid, glycerine, and sugar; and finally, besides all these means, there are a number of others, which have been used upon vague or unintelligible notions, or entirely without any scientific foundation, and which cannot be arranged in any of the groups mentioned. The electric current also, and even transfusion, have not failed of commendation.

It need scarcely be said that the vaunted results of most of these measures are delusive, the fruit of inadequate observations and mistakes of all sorts, to which, indeed, we are so easily exposed in the treatment of diabetes. It has been repeatedly insisted upon in the course of the foregoing exposition, that, without any treatment, the excretion of sugar is subject to many fluctuations; that not only the kind of food, but also the time of its ingestion, is of importance in regard to the appearance of sugar in the urine; that, furthermore, numerous collateral circumstances, psychical affections, bodily exertions, travel, and the like, may have an influence upon it; and it is obvious how easily we may be led to false conclusions if, as is often done, we judge of the action of drugs in diabetes without taking all these circumstances into consideration. Commonly enough, too, especially by the older physicians, no account was taken of the diet of the patients in their therapeutical efforts, and they imputed to the action of drugs changes in the excretion of sugar which it would have been more correct to ascribe to diet. Finally, it is certain that many a drug has deceived a superficial observer by impairing or wholly destroying the patient's appetite, and thus, of course, diminishing his excretion of sugar also.

At the same time, it cannot be denied that a few of the great number of measures recommended have been found by experience to be of service in the treatment of diabetes, even although the theoretical grounds upon which they were recommended have been shown to be to a certain extent erroneous. These means, together with a few others which have attained to a

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[1] *C. Shriver*, in Cincinnati Lancet and Observer. Sept., 1875; and Philad. Med. Times. Sept. 25, 1875. No. 204.

certain importance from their connection with the more recent ideas in regard to the nature of the disease, will be mentioned in the following.

At the head stands *opium.* It was employed even by the oldest physicians (Aëtius), and subsequently in particular by Rollo, J. Frank, Tommassini, and others, sometimes alone, and sometimes in combination with other means, but quite especially by the English physicians, as by Pelham Warren, and was then recommended by M'Gregor and Willis, on the strength of numerous cases in which it effected not only a diminution of the thirst and excessive hunger, but also of the amount of the urine and of its saccharinity. This action has been many times confirmed in more recent times, and especially by Pavy, as well as Kratschmer, by comparative observations with careful reference to the diet ; under its use, even with the mode of life otherwise unchanged, the bodily weight increases. Kratschmer found also in his case a long continued decrease of urea and chlorine, but no alteration in the phosphoric acid in the urine.

Morphia acts in the same manner, as was shown by Kretschy (Duchek), as well as by the observers mentioned, in observations continued through a long period. Of the other alkaloids of opium, only *codeine* is efficient, according to Pavy ; and this, on account of its feeble narcotic properties, should be preferred to opium and morphine. Foster also saw it in one case diminish the quantity and the saccharinity of the urine, but, on account of its unpleasant additional effects (vertigo, etc.), it should be rejected. Pavy observed no effect from *narceine* and *narcotine.*

Benefit may be observed in most cases from the use of opium and morphine, but it is always, or with very rare exceptions, transitory, lasting but a very short time after the use of it is discontinued, and finally ceasing upon its long continued employment. It is advisable, therefore, to employ it only now and then, and especially when the patient is tired of the meat diet and has to return to miscellaneous food, the injurious effects of which may be mitigated by this drug. As regards the method of employing it, it is well not to begin with too small doses, but with moderately large ones, and rapidly increase them until the sugar wholly disappears or is notably diminished, and then discontinue the drug entirely, or, in more obstinate cases, continue the efficient doses for a while longer. It is worthy of note that diabetics bear unusually large doses of opium, as well as of its extracts and morphine. The two former have been given to the amount of seven, fifteen, and even thirty grains a day, and morphine up to several grains, without any further disadvantage being observed than a rather obstinate constipation. This must be overcome by the simplest possible means—enemata, rhubarb, and the like. The benefit of morphine employed subcutaneously has also been ascertained (Kratschmer).

In what way opium and its preparations operate we are not in a position to explain. We should perhaps be inclined to attribute to its action a diminished secretion of the digestive juices and a decrease in the appetite, did not actual observations (made with precisely the same diet before, during, and after the use of opium) afford evidence to the contrary. Neither do the effects of opium upon the nervous system, so far as they are at present known, suffice to explain its favorable action, since other narcotics resembling it and acting otherwise in the same way, such as belladonna, cannabis indica, chloral, and calabar bean, are utterly without effect in diabetes mellitus (Dickinson). From *bromide of potassium* alone has a beneficial effect been observed in a few cases (Begbie and van Traa); but, on the other hand, there is a greater array of cases in which it showed itself wholly inefficient. In mild cases, Foster has found a combination of bromide of potassium with muriated tincture of iron more useful than the former alone.

The *alkalies*, employed now and then by the older physicians on account of acid eructations or a supposed acescence of the juices, were held in great esteem for a time, on the authority of Mialhe. He sought by their introduction into the blood to promote the destruction of the sugar, and to neutralize the volatile acids which were retained in consequence of the defective action of the skin in diabetics. But the expectations raised by him were afterwards very much lowered. In the first place, his theoretical notions were disproved by Lehmann and Bouchardat, and it was also shown experimentally by Poggiale that even large doses of bicarbonate of soda were wholly without influence upon the formation of sugar in dogs.[1] Not much better results were obtained in clinical investigations. Griesinger, who first instituted a methodical investigation of the action of carbonate and bicarbonate of soda in diabetes, saw in two cases out of three a slight decrease in the excretion of sugar, whilst the general health also was somewhat improved. Numerous other observers (Bouchardat, Andral, Kennedy, Lebert, Gaethgens, Gerhardt [Koch], Leube, Foster, Roberts, and Dickinson) have seen sometimes no effect, and sometimes a very slight one, from the long continued use of the drug. The most recent investigations upon this point by Popoff, Kratschmer, and Kuelz have led to still more unfavorable results, for they observed either no effect whatever, or an unfavorable one, from the employment of the agent, which, moreover, is not well borne in large doses. At most, then, we may expect some effect from this drug in the lighter cases, in which perhaps some gastric conditions are present which are improved by the use of alkalies. For the rest, it is worthy of remark that in diabetics the urine is generally slow to become alkaline, even after large and long continued doses of bicarbonate of soda.

Far better results have been observed from the alkaline thermal waters, particularly those of *Vichy*, *Vals*, and *Karlsbad*, which have for a long time, the latter especially ever since Hufeland's recommendation at the beginning of this century,[2] been in great repute for diabetes, and to which Neuenahr has lately been added.

The opinion of the favorable action of these springs, particularly of the Karlsbad, is founded upon the extensive experiience of many physicians—especially, of course, the bath physicians themselves,—according to which, in the first place, diabetics who were excreting sugar on a miscellaneous diet before using these waters, afterwards acquire a greater tolerance of vegetables (of sugar and starch), and secondly, patients who excrete notable quantities of sugar on a purely animal diet, void no sugar at all, or far less, if at the same time they make use of these springs. In the one case, as in the other, the favorable action of the spring continues but for a certain time, sometimes longer and sometimes shorter, and in favorable cases all the symptoms of the disease may, by their repeated use, be made to disappear and its course be very much retarded, especially if in the intervals the patient lead a judicious course of life. At last, however, there comes a time in which these springs, like all other measures, fail. Whether complete recoveries are obtained by the use of any one of the mineral waters mentioned, as is sometimes asserted, we must, for reasons previously mentioned, consider doubtful. It is incorrect also to suppose that only those diabetics are fitted for Karlsbad in whom manifest symptoms of a liver affection or of a plethoric state of the abdominal organs are perceptible. Such symptoms are pronounced in but very few cases, and yet most patients make use of these springs with advantage. (Compare pp. 911 and 954.)

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[1] *Lomikowsky* recently states (Berliner klin. Wochenschr. 1873. No. 40) that he has found that, after the introduction of large quantities of bicarbonate of soda into the stomachs of dogs, the glycogen of the liver is not transformed into sugar, perhaps, as he thinks, on account of destruction of the ferment. *Pavy* had previously observed that destruction of the upper cervical ganglion or its vertebral branch did not occasion any mellituria after injection of carbonate of soda into the blood.

[2] His Journal. 1818. p. 12.

The action of these waters has been chiefly ascribed to the alkalies (the carbonate of soda) contained in them, but whether rightly or not, may, from what has been contributed in regard to the effect of carbonate of soda, seem questionable, and all the more so since no similar results are known to follow from other thermal waters which are very rich in alkalies—those of Ems, for instance. The other constituents have thus far scarcely been taken into consideration, because no effect upon the excretion of sugar was expected from them ; only the sulphate of soda has been examined in this respect by Kratschmer, and found actually ineffectual. Nay, careful observations have been made upon diabetics in hospital by Kretschy and Kuelz with the Karlsbad water itself (the Sprudel and Mühlbrunnen Springs) without any favorable results, and one would therefore be tempted to wholly deny the action of these springs, and particularly of the Karlsbad, which stands in the highest repute, and to impute the results obtained by their means, in so far as they are not accounted for by error due to defective observation, to the account of other contributory circumstances, such as regulation of the diet, a sojourn in the mountain air, freedom from the cares and agitations of daily life, etc. We cannot, however, as Seegen rightly maintains, apply to bathing resorts in general the results of observations of this sort made upon hospital patients, who, for that matter, were very few in number. The conditions which necessarily affect the observations, the restraint imposed upon the patients in their entire mode of life for weeks together, their seclusion, etc., may, and doubtless must, affect their condition unfavorably, and obscure observation. I fully agree with Seegen in attributing greater value in this respect to a large number of good, unprejudiced observations upon patients than to single experiments, apparently exact, instituted upon hospital diabetics under artificial circumstances. Medical experience speaks decidedly in favor of the Karlsbad springs; any physician, even if he has had to treat but a small number of diabetics, will surely have observed now and then an amelioration of the disease under the use of these waters. To be sure, this improvement is not permanent, and not infrequently it lasts but a very short time after discontinuing the treatment. It cannot be denied, too, that a case occurs now and then which is not improved by the Karlsbad springs, for they are no more infallible than is any other agent thus far known.

Lactic acid has been recommended by Cantani, with the view of furnishing to the diabetic, in lieu of the sugar, which remains unemployed in his system, a product of its decomposition. In speaking of the theories of diabetes (pp. 952 et seq.) I have alluded to the possibility that the normal conversion of sugar into lactic acid in the intestine may be interfered with, and have detailed how, in such cases, benefit may be expected from this acid.[1] *We can look for no influence by it upon the morbid*

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[1] *Cantani* himself differs materially, moreover, in his conception of the disease and in the reasons for his proposed treatment, from those here given by me. Thus, for reasons unknown to me, he transfers the formation of lactic acid to the liver, and seeks to spare the action of this organ, by a morbid condition of which the conversion of sugar is hindered, by depriving it of sugar, and furnishing it with lactic acid,—in other words, to afford it rest, and thus bring about a cure. As the liver surely has more to do than to convert sugar (into lactic acid ?), it will be difficult to attain the purpose of giving it rest by depriving it of sugar.

process itself or upon its causes, and therefore it is but erroneous to account it an actual means of cure in diabetes; but it may well be considered, from a theoretical point of view, as the most pre-eminent, or indeed as *the only direct substitute for sugar.* The excretion of sugar is not in any wise altered by the lactic acid, but the patients get the same advantage from the lactic acid that a healthy person gets from starch and sugar, without taking into account the mischievous symptoms to which the presence of an abnormal amount of sugar in the blood gives rise. They may gain in weight, become stronger, etc., and, if they belong to the class in which the sugar disappears from the urine under exclusively animal food, the disease may, by the employment of lactic acid at the same time, be wholly suppressed, and a condition of perfect health take place, without excessive ingestion of food. In this way we may explain the favorable results observed by Cantani himself, as well as by Balfour and Foster; and in like manner it is easy to understand how others, as Ogle, Seegen, Kuelz, and Popoff (who used lactate of iron), were unable to observe any influence upon the excretion of sugar, for this indeed does not depend upon the lactic acid, but upon the constitution of the food and the nature of the individual case. According to Cantani, from 75 to 150 grains of the acid should be taken daily, in from 8 to 10 fluidounces of water. Larger quantities are apt to give rise to diarrhœa, and in certain cases ("rheumatic") pains in the joints have been observed to occur after its protracted use, which speedily disappeared on discontinuing the medicine (compare "Polyarthritis Rheumatica Acuta," p. 28). On grounds similar to those which sustain the use of lactic acid, one might also recommend the *fatty acids* of ordinary fatty food, *oleic*, *palmitic*, *stearic,* and *butyric acids*, etc., which have not yet been used for this purpose. The fats themselves (glycerides), indeed, contain besides these fatty acids, glycerine, which is set free in the intestine by the influence of the pancreatic juice, and is changed into glycogen in the liver; consequently they must do harm in certain cases (previously described, pp. 955 et seq.). It would be difficult to entirely divest the food of them, *but nevertheless their ingestion may be limited, and they may be* *partially replaced by the fatty acids.* Since it has been shown by Radziejewski,[1] that animals may be fattened by feeding them with meat free from fat and with soaps, that they accumulate fat, whilst deriving the glycerine necessary for its formation from some other source, either from the meat eaten or from the body itself, or form it *de novo;* therefore, by giving to a diabetic, to whom glycerine is injurious, fatty acids (together with meat, of course), we afford him the advantages of the fat without its disadvantages, just as we make the sugar available to him by means of lactic acid. The fatty acids would be particularly indicated in all cases in which there was degeneration of the pancreas (p. 887). A *curative* of the disease is, however, no more to be found in them than in lactic acid.

This is the proper place to call attention to the fact that *cod-liver oil* has often been employed with benefit in diabetes, both formerly and of late years (Thompson, Hogg, Babington, and Salomon[2]), and even vaunted as a curative. It contains, together with glycerides, *free fatty acids in considerable amount*, and it is to these in particular that Buchheim[3] recently ascribes the efficacy of cod-liver oil, which is far greater than that of other fats, in various morbid conditions. In diabetes, in which the ingestion of the glycerides as *drugs* is superfluous and may be injurious, the fatty acids as such always deserve the preference.

In two cases I have employed partly cod-liver oil and partly pure fatty acids in the form of soap (seven scruples of soap, to be made into sixty pills with a few drops of mucilage; of these from four to five are to be taken three times a day); these cases, however, did not admit of strict control, because no adequate regulation of the daily diet as to quantity and quality could be had. In one of the cases it was only noticed that, with a diet unrestricted in quantity, but with a preponderance of meat, using at the same time from one to two tablespoonfuls of cod-liver oil and twelve of these pills daily, the excretion of sugar remained about the same as with the same sort of diet without the cod-liver oil and pills, but that the bodily weight was rather rapidly increased (*i. e.*, about eleven ounces in fourteen days). In the second case, treated at the Polyclinic, the patient walking about, the soap-pills alone were employed (12–15 daily), to the use of which the patient at first thought he could ascribe a diminution of the thirst and hunger. There were no digestive disturbances, in spite of their being used for several weeks.

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[1] Virchow's Archiv. XLIII. p. 268. Compare also *Kuehne*, Lehrb. der physiol. Chemie. p. 377.

[2] Med. Centralztg. 1857. 25 Nov.

[3] Archiv f. exper. Pathol. und Pharmakol. III. p. 218.

To arrive at a well-founded opinion in regard to the practical value of the fatty acids, we must entirely deprive the diabetic of fats, or limit him to a small, accurately ascertained quantity daily, whilst the diet remains constantly the same in other respects, and then, after a sufficiently long preparatory period, add the fatty acids to this diet, in order to determine their influence upon nutrition, bodily weight, and capacity for work. Or else, in patients who excrete sugar upon a diet consisting only of albumen and fat (with extractive matters, salts, and water), we must replace the fat, wholly or in part, by fatty acids, and test the accompanying behavior of the excretion of sugar. Either of these plans, of course, meets with great impediments in practice.

Glycerine also has been recommended by Schultzen, not as a means of curing diabetes, but as a *substitute* for sugar, upon the ground, to be sure, of the false, or at least wholly unproved, theory that in healthy persons sugar is decomposed into glycerine and aldehyde of glycerine (compare p. 950, note). Schultzen's proposition is, however, superfluous at least, even apart from his theory, for his purpose is accomplished already by giving fat. It is remarkable that he overlooked this, and still more remarkable that his statements have given rise to so lively a conflict in regard to the value or worthlessness of glycerine, whilst not the least doubt has thus far been raised in regard to the value of the fats, but they have been universally accounted very useful. It is obviously inconsistent to regard the fats as harmless or even beneficial, but glycerine as detrimental, and *vice versa*. I have already (p. 985) characterized the fats, for the very reason that they contain glycerine, as an article of food not wholly harmless, but only conditionally allowable, which necessity compels us to allow, since it cannot be withheld without greater injury resulting. It is quite certain that many diabetics eat fat with impunity and even with benefit to their nutrition, because they are able to assimilate a certain amount of hydrocarbons. In such patients glycerine, too, within certain limits, will remain without influence upon the excretion of sugar; and, if their food be wholly deprived of fat, they are able to bear still greater quantities of it. Perhaps they may even bear larger amounts of glycerine than of sugar, for it is to be assumed that two molecules of glycerine ($C_3H_8O_3$) must always unite to form one molecule of sugar ($C_6H_{12}O_6$) or glycogen ($C_6H_{10}O_5$). Thus perhaps are to be explained those cases—rare, to be sure, but which still certainly do occur, as observed by Schultzen (Harnack), Foster, and van Traa—in which glycerine proves less injurious than other hydrocarbons, in that under its use the excretion of sugar not only does not increase, but even diminishes. At any rate, I know of a case in which vegetable food augmented the saccharinity of the urine, but glycerine did not. To this extent, then, we may allow that glycerine is preferable to sugar, as being the less injurious substance, and perhaps we may profit from it in practice in many cases, especially in preparing food for patients who are unwilling to dispense with all sweets. But even in this respect it is excelled by mannite (p. 989), and in all other regards we must let the glycerine which is taken in with the fat suffice for the patient. The importance of this agent in the treatment of diabetes amounts, therefore, to nothing at all. If any one wishes to give it in cases of the sort described, *i. e.*, in patients who have not yet lost all power to assimilate hydrocarbons, as a generator of force in place of sugar, it is advisable to add a little tincture of opium to it, as in tolerably large quantities it is apt to provoke diarrhœa.

The supposition that abnormal fermentative processes lie at the foundation of diabetes has recently induced Ebstein and Jul. Mueller to employ *carbolic acid*, as it formerly led to *creasote* being recommended (Berndt, Hufeland, Corneliani, and others). Although this hypothesis has nothing whatever to rest upon, and is not very probable, still carbolic acid has already, during the short time since it was introduced into the treatment of diabetes, produced some results. Besides Ebstein and Mueller, Kraussold and Boese have seen benefit, although but slight, from its use; whilst in other cases, it is true, it was wholly abandoned by Ebstein and Mueller themselves, and by Diehl and van Traa. At all events, it seems to be worthy of further trial. That the anti-fermentative property of the carbolic acid is not to be considered also follows from the fact that *salicylic acid*, according to a later contribution by Ebstein, is wholly inefficient. The opposite of this method is exemplified in the old experiments with *yeast*, and in the more recent observations of Kussmaul, who saw the amount of sugar in the urine decrease after the injection of *diastase* into the blood (but not into the subcutaneous cellular tissue).

Arsenic was long since recommended by Berndt, and in more recent times by Devergie, as well as by Leube—by the latter from remarking the decrease of glycogen in the liver, proved by Laikowsky to take place in animals poisoned with arsenic. In a certain number of cases the drug has really diminished the excretion of sugar, but in others it has not, without the reason of this varying action being apparent.

In three cases Seegen has seen the sugar entirely disappear from the urine after giving from 20 to 30 drops of *tincture of iodine* daily, but it immediately reappeared on suspending the remedy. Formerly *iodide of potassium* was frequently vaunted in diabetes, but, like so many other drugs, was neglected again.

Blumenthal saw a strikingly favorable result in one case (which had resisted codeine, tannic acid, and other means) from *quinine* (six to thirty grains of the muriate daily). Diehl also saw the excretion of sugar considerably diminished in two cases under the use of quinine. It may be mentioned, in addition, that Carlatti[1] states that he cured a diabetes with *eucalyptol.*

Finally, the *preparations of iron* were long ago recommended, partly as a specific (especially the phosphate of iron, according to Venables), and partly as in general improving the constitution of the blood and increasing the nutrition.

To sum up all that has been said in regard to the treatment, we find that in any case of diabetes we must first regulate the diet according to the fundamental points above given, and that so long as the prescribed diet suffices to hold the symptoms in check and is well borne, and furthermore, so long as the strength has not suffered very much, we may abstain from all drugs. It is best to allow periods of moderately stringent diet to alternate with periods of a perfectly strict diet, and with those of a less restricted choice of food. At the time of the most stringent limitation the administration of lactic and fatty acids is to be recommended, to cover the deficiency of nutritive substances. In the next place, a residence of several weeks during the summer at Karlsbad, Neuenahr, or Vichy, may be tried, which affords patients, together with the beneficial influence of the waters, the further advantages of remaining in the open air, the avoidance of excitement, and the like. So soon as diet alone fails in its effect, or from any cause whatever cannot be quite strictly adhered to, some one of the drugs mentioned is to be tried, and in particular, as being the surest, opium or one of its preparations, especially morphine, then quinine carbolic acid, arsenic, or whatever other one may be preferred.

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[1] Schmidt's Jahrb. 1873. CLVII. p. 235.

The digestive organs always demand special attention, and their derangements are to be combated, according to special indications, by alkalies or bitter and astringent agents. If a decline in the strength becomes notable, tonic medicines, such as iron and quinine, may be employed.

Complications likewise require, so far as comports with their treatment in other respects, the greatest possible care in regard to the diet. It should be specially mentioned that *affections of the mouth*, particularly caries of the teeth, should be prevented and combated by the use of alkaline mouth-washes (solutions of carbonate of soda, lime-water, and weak soap-water); and also that, according to the view of many surgeons, *operations* upon diabetics should be undertaken only under the most extreme necessity, and with particular caution, on account of their great liability to gangrene.[1]

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[1] Compare *Verneuil*, Gaz. des hôpit. 1866. Nos. 143 et seq., and Union méd. 1866. No. 142.

Appendix.

As considerable time elapsed between the preparation of the article on Diabetes Mellitus and the publication of the volume, I will add here, as an appendix, the most important of what has in the interim come to my knowledge in regard to the disease in question.

To p. 867.—Further cases of diabetes observed in childhood: *Rossbach* (Berliner klinische Wochenschrift. 1875. No. 22), in a *girl* seven months old, after a fall; death after three months.—*Benson* (Brit. Med. Journal. 1875. No. 773), in a boy four years old; death after four weeks.—*Donkin* (Lancet. 1875. Vol. II. No. XXV.), in a girl ten years old, resulting in recovery by the use of skimmed milk. In all, therefore, of 33 children under 15 years of age, there are 20 girls and 13 boys.

To p. 883.—*Fürbringer* (Deutsches Archiv f. klin. Med. XIV. p. 499) found in a diabetic patient who died at *Friedreich's* Clinic, along with broncho-pneumonic collections in the left lung, cavities with ragged, greenish brown, inodorous contents, which enclosed numerous fibres of aspergillus.

The central nerve-parts, the cœliac ganglia, and splanchnic nerves showed neither gross nor microscopic changes.

To p. 888.—After *Cowley*, the formation of calculi in the pancreas was found by *Elliotson* (Med.-Chir. Transactions. XVIII. London, 1833. p. 67)—atrophy or fatty degeneration of the same organ, in addition, by *Silver* (Transact. of the Pathol. Soc. XXIV. 1873), *Friedreich* (see this Cyclopædia. Vol. VIII.), *Haas* (Bericht aus der Klinik des Prof. *Jacksch*, in Prager Vierteljahrschr. CXXX. 1876. p. 144).

To p. 891.—According to a preliminary contribution of *Cantani's* (Moleschott's Unters. z. Naturlehre. XI. H. 5. p. 443), the sugar in the blood of persons suffering from diabetes differs from that of the urine (grape-sugar) in its having no influence upon polarized light.

To p. 907.—*Reichard* (Fresenius' Zeitschr. für analyt. Chemie. 1875. XIV. p. 417) saw dextrine (glycogen?) appear in the urine of a diabetic after the disappearance of the sugar.

To p. 908.—*Krusenstern* (Virchow's Archiv. Bd. LXV. p. 410) sought in vain for *cholesterine* in the urine of diabetic patients. *Fürbringer* (l. c.) also found *oxalic acid* for a length of time in the urine of a person suffering from diabetes.

To p. 913.—*Fürbringer* found crystals of *oxalate of lime* during a long time in the above-mentioned patient. A short time before death *filaments of aspergillus* and *needles of fatty acid* were found in the same sputum.

To p. 916.—*Berti* (La France médicale. 1874. No. 94) also observed sudden death, which was attributed to acetonæmia.

To p. 917.—In regard to the affections of the eye occurring in diabetic patients, see *Leber*, in v. Graefe's Archiv. Bd. XXI. Abth. 3.

To p. 933.—*Ewald* also has found (Berliner klinische Wochenschrift. 1875. Nos. 51 and 52) that the blood of non-diabetic persons contains sugar.

To pp. 935 and 985.—According to *Kuelz* (Marburger Sitzgsber. 1876. No. 4. Mai), *inosite* also is without influence upon the formation of glycogen in the liver.

To p. 942.—No sugar appears in the urine after poisoning with nitro-benzole, as *v. Mering* has shown (Centralblatt für die med. Wochenschrift. 1875. p. 945); in its stead, however, is found a substance, reductive indeed, but which turns polarized light to the left, and is not susceptible of fermentation.

To p. 974.—In applying Trommer's test in the manner described, in the absence of sugar, a reduction may occur owing to the presence of "pyrocatechin," which is occasionally observed in the urine. To avoid mistakes, we may filter the urine with acetate of lead, and apply the test to the filtrate (see *Fürbringer* [Berliner klinische Wochenschrift. 1875. Nos. 24 and 28]).

To p. 1002.—*Jacobs* likewise found transient benefit from *glycerine* (Virchow's Archiv. LXV. p. 481). *Carbolic acid* was first employed with a favorable result by *Orson Millard* (according to *Blau*, in Schmidt's Jahrbüchern. CLXVIII. p. 81), and *Thoresen* likewise saw a beneficial effect from it (Schmidt's Jahrbücher. CLXIX. 1876. 123). In contrast with salicylic acid, *Ebstein* found *salicylate of soda* of some service (Berliner klinische Wochenschrift. 1876. No. 24).

To p. 1003.—*v. Pap* found arsenic useful in mild cases (Wiener med. Presse. 1875. Nos. 13 und 14); *J. Mayer*, *quinine*, whilst *Ebstein* and *Mueller*, as well as *Kratschmer*, employed it without effect.

DIABETES INSIPIDUS.

Literature.

The earlier literature down to the time of Thomas Willis, as well as a considerable part of the later literature, is the same as that of Diabetes Mellitus, to which therefore the reader is referred.

Sauvages, Nosol. methodica. Amstelodami, 1763. III. p. 184.—*Michaelis Ettmulleri* opera omnia. Lugduni, 1687. pars secund. p. 188.—*Joannes Oosterdyk Schacht*, Institutiones med. pract. 1767. p. 246.—*Haller*, Elementa physiol. corp. humani. Laus. 1778. VII. Diabetes.—*R. A. Vogel*, Academicae praelectiones de cognoscendis et curandis corporis hum. affectibus. Goett. 1772. p. 279 f.—*W. Cullen*, First Lines of the Practice of Physic. Edinburgh, 1810.—*M. Troja*, Ueber die Krankheiten der Nieren. Aus d. Ital. 1788. S. 205.—*P. Frank*, De curandis hominum morbis epitome. 1792. Classis V. § 479.—*W. Prout*, Inquiry into the nature and treatment of diabetes, etc. II. edit. London, 1825. p. 187 et seq.—*R. Willis*, Urinary diseases and their treatment. London, 1838. Deutsch. 1841. S. 28 ff.—*L. U. Lacombe*, L'Expérience. Journ. de méd. et de chir. 1841. p. 203, und De la Polydipsie. Paris, 1841.—*C. Novellis* (Giornale di Torino), Schmidt's Jahrb. LII. 1846. S. 308.—*Voigt* (Schweiz. Cantonztschr.), Schmidt's Jahrb. 1847. LIII. S. 295.—*Fleury*, Arch. gén. de méd. 1848. Mai.—*Falck*, Beiträge zur Lehre von der einfachen Polyurie. Deutsche Klinik. 1853. No. 41.—*Bernard*, Union méd. 1853. p. 153.—*C. Weber*, Ueber D. insip. Diss. Würzburg, 1854.—*C. Baudin*, De la polydipsie et quelques mots sur la polyurie. Thèse. Paris, 1855.—*Poggiale*, Gaz. méd. de Paris. 1854. No. 33.—*Trousseau*, Union méd. 1855. No. 18 und Clinique méd. Deutsch. 1868. II. S. 748 ff.—*Th. Neuffer*, Ueber D. ins. Diss. Tübingen, 1856.—*Edm. Neuschler*, Beiträge zur Kenntniss der einfachen und der zuckerführenden Harnruhr. Diss. Tübingen, 1861.—*Al. Andersohn*, Beiträge zur Kenntniss der nicht zuckerführenden Harnruhr. Diss. Dorpat, 1862.—*Landouzy*, Clinique de l'hôtel Dieu de Reims. Paris, 1862. S. 13.—*Fischer*, Arch. gén. de méd. 1862. II. p. 418.—*Magnant*, Du Diab. insip. Thèse. Strassburg, 1862.—*Kiener*, Essai sur la physiologie de la

polyurie. Strassburg, 1865.—*E. Leyden*, Ein Fall von D. insip. Berliner klin. Wochenschrift. 1865. Nr. 37.—*Lasègue*, De l'état actuel de nos connaissances sur la polyurie. Arch. gén. de méd. 1866. II.—*Maumené*, Sur le D. non sucré. Comptes rendus. 1866. LVII. p. 989.—*Kien*, De l'hydrurie. Gaz. hebdom. de méd. et de chir. 1866. p. 163 ff.—*Crapart*, De la polyurie. Thèse. Paris, 1866. *Roger*, Polydipsie chez les enfants. Journ. de méd. et de chir. prat. 1866. p. 138.— *Reith*, Polydipsia. Treatment by large doses of valeriana. Improvement. Med. Times and Gaz. 1866. I. p. 209.—*F. Mosler*, 1) Ueber Harnanalyse von D. insip. Inosurie mit Hydrurie. Virch. Arch. XLIII. S. 229. 2) Neuropathische Entstehung der einfachen Harnruhr (Hydrurie), etc. Ibidem. LVI. S. 44.—*Lancereaux*, De la polyurie. Thèse. Paris, 1869.—*Bemiss*, Polyurie s. Virchow's und Hirsch's Jahresber. 1869. II. S. 259.—*Bourdon*, Polyurie simple avec anthrax. Gaz. des hôpitaux. 1869. No. 17.—*F. Strauss*, Die einfache zuckerlose Harnruhr. Tübingen, 1870.—*A. Pribram*, Untersuchungen über die zuckerlose Harnruhr. Prager Vierteljahrschrift. 1871. CXIII. S. 1.—*Kuelz*, s. Diab. mell.—*Guéneau de Mussy*, Etudes sur le traitement de la polyurie Gaz. des hôp. 1871. No. 98.— *Bradbury*, Case of D. ins., rapid improvement under the use of Valeriana. The Lancet. 1872. I. No. 2.—*Massot*, Note sur un cas de tumeur cérébrale avec polyurie. Lyon méd. 1872. No. 15.—*F. Buerger*, s. Diab. mell.— *W. Ebstein*, Ueber die Beziehungen zwischen Diabetes insip. zu Erkrankungen des Nervensystems. Deutsches Arch. f. klin. Med. XI. S. 344.—*E. Schlesinger*, Zur Kenntniss des D. ins. Diss. Berlin, 1874.— *W. H. Dickinson*, Diseases of the kidney, etc. I. London, 1875. p. 180.—*H. A. H. van der Heyden*, Diab. ins. Diss. Leyden, 1875.

Introduction and Historical Survey.

The name *Diabetes insipidus* or *Polyuria* (Hyperuresis, Urinæ profluxio, Polydipsia) is applied to every chronic, morbidly increased excretion of urine, free from sugar, which is caused by no profound structural changes of the kidney, and which constitutes either the sole or at least the most prominent and primary morbid phenomenon.

Before the discovery of sugar in the urine., *i. e.*, down to the time of Thomas Willis (1670), it was of course impossible to distinguish between Diabetes mellitus and Diabetes insipidus. Physicians included all cases of chronic increase of the urinary excretion under the general term *Diabetes*, although differences in their progress and results had not escaped notice. Even long after the time of Thomas Willis no distinction was made between the different forms of diabetes according to the presence or absence of sugar in the urine, partly because a knowledge of the discovery was not widely spread among physicians, and partly because, ignorant of the importance of sugar in the animal economy, they failed to appreciate its bearing. They either continued to speak of only *one* kind of diabetes, or they recognized a *true* diabetes, in which the fluids swallowed were supposed to pass through and to be excreted unchanged from the body; and a *false* diabetes, in which it was thought that a liquefaction of the tissues of the body took place, causing the excreted to exceed the ingested fluids in amount. This distinction, originating with Ettmueller (about 1680), dependent upon a supposed difference in the relation of the ingested water to that excreted with the urine, was maintained for nearly a century by the most distinguished medical writers of the period (Borsieri, R. A. Vogel, Trnka de Krzowitz, Oosterdick-Schacht, and others). The presence of sugar in the urine was either not alluded to or was treated as a matter of secondary importance. Many authors (Borsieri, Trnka de Krzowitz, Darwin[1]) described a *Diabetes chylosus*, in which they supposed that the chyle found its way into the urine, thus accounting for its sweet taste.

Not till the middle of the eighteenth century did Sauvages describe the excretion of sweet (saccharine) urine as a special form of diabetes (*D. anglicus*). This author, however, still recognized a form of diabetes characterized by greater excretion than ingestion of water (*D. legitimus Aretæi*), and also described five other rather arbitrarily adopted forms of the disease (*D. hystericus*, *D. artificialis*, produced on dogs by Malpighi by ligature of the splenic veins, *D. a vino*, *D. arthriticus*, *D. febricosus*). It was not till towards the end of the eighteenth century that the presence of sugar in the urine was assumed by Cullen, and especially by P. Frank, as the only basis of classification, and diabetes divided into *mellitus* (henceforth also called verus) and *insipidus* (spurius). Since that time both these forms have been universally recognized by pathologists, but their association has in the course of time become much less close. For the numerous investigations undertaken in this century have led to the conviction that diabetes mellitus is a disturbance of nutrition of a special sort, and is to be regarded as an independent disease running its course with a definite train of symptoms, while, in regard to the pathological position of diabetes insipidus great doubt still prevails, because under this term are included various conditions which resemble each other neither in their origin nor in their appearance nor in their anatomical changes.

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[1] *Salomon.* Geschichte der Glycosurie. l. c., p. 560.

Robert Willis, a countryman of his namesake of one hundred and fifty years before, pointed out that when the total amount of urine is increased, the proportion of the solid constituents may vary very greatly ; that the *urea* especially may be excreted, sometimes in normal, sometimes in excessive, and sometimes in diminished amount. He therefore recognized various forms of polyuria, viz., *Hydruria*, in which the excretion of water only is increased; *Azoturia*, in which an excessive amount, and *Anazoturia*, in which little or no urea is excreted. This subdivision has been adopted by many writers entirely unchanged, or with only a change of names, while others have accepted it only in part. J. Vogel, for instance, has retained the term *Hydruria* in the sense given to it by R. Willis ; but, on the other hand, he uses the term *Diabetes insipidus* in a narrower sense to indicate a condition characterized by an increase of some or all of the solid constituents of the urine—a classification which has also been adopted by recent French authors (Kiener, Kien). From a purely theoretical point of view, this classification might perhaps appear justifiable. In fact, it might even appear perfectly natural if, as has already been done, diabetes in its narrower sense were still further subdivided into different varieties, according to the special constituent which is increased in amount—not only, therefore, into *azoturia* and *anazoturia*, as Willis proposed, but into polyuria with increase of the coloring matter, of phosporic acid (*Phosphaturia*), of oxalic acid (*Oxaluria*), etc. But this is a classification by which pathology is enriched only by a number of empty columns with names of diseases, but without the diseases themselves which belong there. Not that such an abnormal increase of some or all of the urinary constituents does not in reality occur ; on the contrary, we know that all these constituents are, under certain circumstances, very much increased (and also diminished). We can even connect occasional disturbances, certain morbid phenomena, with these anomalies of excretion ; but it is impossible to regard them as bearing a fixed relation to any special, well-defined and always recognizable form of disease, because they are secondary phenomena in other more or less well-known morbid processes, or because they disappear in the complex grouping of the symptoms. *Azoturia*, *Oxaluria*, *Phosphaturia*, etc., are symptoms whose discovery and consideration may in many cases be very important, but the conception of definite diseases cannot as yet be connected with them, just as we do not at present regard albuminuria as a definite disease. In the same way *diabetes insipidus*, in Vogel's meaning of the term, cannot be regarded as a separate form of disease and distinguished from *Hydruria*, for it is by no means proved that each of these varieties arises and runs its course separately ; on the contrary, it seems that the proportion of the solid constituents may vary greatly in every single case, and it is therefore impossible to connect with each variety a special characteristic train of symptoms.

We do not attempt, therefore, to divide *Polyuria*, occurring as an independent morbid process, into varieties, although we do not deny the existence of differences in the relative amounts of the various urinary constituents. We prefer, however, for the more independent disease the name *Diabetes insipidus*, in order to distinguish it from other conditions with which an increased excretion of urine is associated.

These conditions are, as is well known, very numerous, and it is therefore important to exclude them, as we have done above, in forming the conception of the disease which here occupies our attention. The cases which remain after this exclusion we must, for the present, include under the term Diabetes insipidus, postponing till some later time a further limitation of its range according as the dependence of the characteristic symptom of this group, the increased excretion of urine, shall receive a further etiological or anatomical explanation.

In limiting the term Diabetes to a *morbid* increase of the urinary excretion, we have excluded any increase which is caused by *excessive ingestion of fluids*, by the *use of diuretics*, or by interference with the *loss of water through the lungs and skin;* for all these circumstances cause also in healthy individuals an abnormally large excretion of urine. For the same reason also we cannot regard as diabetes that more or less persistent increase of the urinary excretion which occurs during the absorption of watery exudations, because here, just as in the case of increased ingestion of water, we have a purely physiological process, consisting in the emptying of the vascular system which has been abnormally filled by the absorbed fluid, and because, moreover, the increase of the urinary excretion is here not the primary symptom, but a conservative phenomenon dependent upon morbid conditions of other organs. Upon similar processes depends also, at least in part, that increase of urine which is not infrequently observed in *convalescence from febrile diseases.* Here we must, in the first place, consider that during the fever there is often, owing to the imperfect action of the kidneys, an accumulation of urea in the body. This urea is excreted after the cessation of the fever, and by means of its specific diuretic effect causes at the same time an increased excretion of water by the kidneys. The diuresis caused by the urea is increased also by the action of the sodic chloride, which, as is well known, is present in the urine only in very small amounts during the febrile condition, but in convalescence is greatly increased chiefly in consequence of its greater ingestion with the food (Salkowski [1]). In the second place the condition of hydræmia ("Subalbuminosis" of the blood), which prevails in convalescence, has an influence in increasing the urinary excretion; and, finally, the greater excretion of water depends also *perhaps* upon the circumstance that during the fever there is a retention of water in the body, which on the cessation of the disease is removed by the greater activity of the kidneys, and also upon the fact that non-nitrogenous substances (*fats*), which in fever arise from the decomposition of albumen and are retained in the body, are afterwards oxidized, and increase the amount of water in the body.[2]

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[1] Virchow's Archiv. LIII. p. 209.

[2] Cf. on all these points: *Senator*, Untersuchungen über den fieberhaften Process, etc. 1873. pp. 92–117.

From what has been said above, it is evident that the increase of the urinary secretion, which is observed as a more or less persistent *symptom of certain renal diseases*, is not to be regarded as diabetes insipidus. Formerly, when the anatomical changes of the kidneys were less understood and less accessible to diagnosis, polyuria dependent upon chronic renal disease was undoubtedly very often regarded as diabetes insipidus, as is evident from many data of post-mortem examinations.

In the same way it is evident that the temporary increase of the urine, which often occurs in *hysteria or other diseases of the nervous system* as a phenomenon of secondary importance in the train of symptoms belonging to other organs, is not usually to be regarded as diabetes insipidus. Here, however, the distinction is not always readily made, and if the symptom of polyuria becomes more prominent by its intensity or its duration, or by its effects, as increased thirst, etc., it is customary to designate it as diabetes insipidus, especially since in recent times attention has been called to the connection of this disease, and also of diabetes mellitus, with affections of the nervous system, and there is a strong tendency to regard diabetes insipidus in general as a nervous disease.

Finally, the relation of diabetes insipidus to *Polydipsia* must be referred to. Lacombe, and after him a number of French physicians (Baudin, Magnant), regard as the starting-point of all the phenomena in the train of symptoms of diabetes insipidus, an abnormal increase of the feeling of thirst, which leads to the ingestion of an immoderate amount of water, and its excretion through the kidneys. It will be shown hereafter that this view is, at least for the majority of cases, incorrect. It is, however, not impossible that a primary polydipsia may exist as the result of a disturbance of the thirst-perceiving nervous apparatus, the peripheral channels of which are, according to Romberg,[1] to be found in the œsophageal branches of the vagus. For such extremely rare cases the term Polydipsia may be retained, while it is inapplicable to the far more numerous cases in which thirst occurs undoubtedly only as a result of increased renal activity.

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[1] Lehrbuch der Nervenkrankheiten. I. p. 123, and Klinische Wahrnehmungen und Beobachtungen. Berlin, 1851. p. 8.

Etiology and Pathogeny.

There are no trustworthy statistical data as to the frequency of diabetes insipidus as compared with other diseases and causes of death, for the duration of the malady, which is usually considerable, makes it difficult to follow a single case to the end, and the result is, on the whole, not often fatal. It is therefore not easy to determine its relation to disease and mortality in general. It can only be stated in a general way, that diabetes insipidus is not a common, but yet not an extremely rare disease.[1]

Age seems to have some influence on the occurrence of the disease, for it is observed much more frequently in youth and in middle age than in later life. Even in the new-born child the disease is said to occur (Dickinson). Its distribution in the different periods of life is shown in the following tables compiled by Roberts[2] from 70, by Strauss from 85, and by van der Heijden from 87 cases in which the age is given :

Age.	Roberts.	Strauss.	van der Heijden.
Less than 5 years	7	9	2
5–10 "	15	12	5
10–20 "	13		19
20–30 "	16	57	23
30–40 "	—	—	19
40–50 "	15	—	9
50–60 "	—	7	6
60–70 "	4	—	4
	70	85	87

Similar relations are shown by the earlier, less extensive compilations of Lancereaux, Neuffer, Laccmbe, and Strauss. In regard to *sex*, Roberts records, out of 77 patients, 55 male and 22 female ; van der Heijden, out of 96 patients, 71 male and 25 female ; so that males are from two to three times as numerous as females. Whether the difference of sex is manifest in childhood is doubtful. Neuschler records at the age of 0-10 years, 6 male and 3 female; at the age of 10-20 years, 3 male and 3 female patients. On the other hand, in the compilation of van der Heijden are to be found at the age of 10 years and under, 3 male and 4 female, and between 10 and 20 years, 12 male and 7 female patients.

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[1] The only positive datum is that of *Forget* (Résumé clinique de juillet, 1842, à juillet, 1844, according to *Strauss*, l. c., p. 52), that amongst 1,000 patients of all sorts, 3 cases of "Polydipsia" were observed.

[2] On urinary and renal diseases. 2d edition. According to *Dickinson*, l. c.

An *hereditary predisposition* has been proved to exist in several cases. The most remarkable, but somewhat fabulous, instance is that related by Lacombe, in which out of one family a mother, three sons, and a daughter were attacked by the disease, besides the brother of the mother, and his children. Less remarkable, but well authenticated cases, in which two or more blood-relations suffered from diabetes insipidus, are reported by Lancereaux, Deebray, Reith, Desgranges, and Addinel Hewson.[1] An hereditary connection with *diabetes mellitus* has also been sometimes observed. Thus, Trousseau reports the case of a female patient nineteen years old, whose grandfather suffered from diabetes mellitus. Reith records that of a woman twenty-four years old, whose father and brother had had this disease, and Seegen, on the other hand, describes the case of a patient with diabetes mellitus whose father suffered from diabetes insipidus. Finally, attention has been recently called to the occurrence of diabetes insipidus as well as of diabetes mellitus in persons of *neuropathic* and *psycopathic predisposition.*

As *exciting causes* are to be regarded, in a certain number of cases, *injuries of the skull*, violent and sudden *emotions*, *chronic diseases of the brain and spinal cord*, and a single *excessive ingestion of cold beverages or other fluids*. Among all these causes the affections of the nervous system possess a special interest on account of the dependence of the excretion of urine upon nervous influences and on account of the analogy with the increased urinary excretion which can be experimentally produced and which will be presently described. A fact worthy of especial emphasis is that in a considerable number of cases the lesion of the central nervous system causing diabetes insipidus was in the *medulla oblongata or on the floor of the fourth ventricle*, as was in part proved by the autopsies and in part inferred from the phenomena of the disease (Cf. Mosler, Ebstein).

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[1] American Journal of Med. Sciences. 1858. p. 379.

In addition to these causes, colds of all sorts, previous acute or chronic diseases, abuse of spirituous liquors, and violent exertions are regarded with more or less probability as giving rise to the disease. In a considerable number of cases no immediate cause for the disease can be shown.

Cases of diabetes insipidus which have arisen immediately after a *concussion or injury of the skull* have been reported by Fischer, Golding Bird,[1] Charcot, Mosler, Bemiss, Moutard Martin, Debrou, and others. The disease has also been known to occur in isolated cases after injuries to other parts (*e. g.*, after a blow in the hepatic region, Piorry, Trousseau); but here fright also plays doubtless an important part. Cases of the disease following concussion of the brain have also been reported by Hadra (Dissertation. Berlin, 1866. Case in Frerichs' Clinique), and by H. Fischer (On Commotio Cerebri in Volkmann's Collection of Clinical Lectures. No. 27. 1871. p. 133). In one case (Fischer's) the urine contained sugar during the first five days.

Violent muscular effort was regarded by Jarrold (Recherches sur le D. ins. in Bibliotheca med. XX. Paris. 1808. p. 278) as a cause of the disease.

Violent emotions occasioned the disease in a case reported by Lacombe, perhaps also in one of those recorded by Kuelz (Beiträge II., p. 28).

New formations in the brain, extravasations of blood or inflammatory and degenerative conditions giving rise to the disease, have been observed by Weber (Jaksch), Kien, Leyden, Mosler, Roberts, Lancereaux, Pribram, Strauss, Luys, Dickinson, Ebstein, and Van der Heijden (Rosenstein).

A connection with *epilepsy* was noticed by Massot in one case, by Ebstein in two cases, and I have myself seen two such cases in Traube's Clinic. Similar observations have also been made by Handfield Jones (Med. Times and Gazette, 1875. No. 1328).

As the result of *chronic disease of the spinal cord*, diabetes insipidus has been observed by Traube (Vide Gesammelte Beiträge zur Pathologie und Physiologie. II. p. 1048, and Schlesinger, Diss. p. 32), and I have myself also observed a case of this sort. In one of Mosler's cases the disease developed itself several years after recovery from *cerebro-spinal meningitis*.

Temporary increase of the urinary excretion is frequently observed also in acute affections, especially in the course of and in recovery from cerebro-spinal meningitis; but this is not regarded as diabetes, on account of its short duration. That the usually very transient polyuria occurring in cases of hysteria is also not to be considered as diabetes, has been already stated (see p. 1013); but the possibility is not thereby lost sight of that diabetes insipidus may be associated with hysteria (as in cases reported by Debout and by Kuelz).

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[1] Lancet. 1839-1840. Vol. I. p. 843.

In order to understand how a persistent morbid increase of the urinary excretion can take place *without any disease of the kidneys* (for only under these circumstances is the term Diabetes insipidus applicable), it is necessary to consider the physiological conditions under which the urine is excreted. According to our present knowledge, apart from changes in the kidney and the urinary tract, the following circumstances affect the amount of the urinary excretion :

(1). The pressure under which the blood flows into the renal arteries ; with the increase of this pressure increases, other things being equal, the amount of urine excreted in the unit of time.

(2). The nature and composition of the blood-plasma. The excretion is increased, in the first place, by an abnormal amount of water in the blood ; and, secondly, by an abnormal quantity of diffusible and diuretic substances, such as urea, sugar, and certain salts.

(3). Peculiar nervous influences affecting the excretion, probably independently of the *general* blood-pressure. In regard to this subject, Cl. Bernard, as is well known, was the first to make the statement that an injury to the floor of the fourth ventricle, just above the point where irritation causes glycosuria, very often produces an increased flow of urine, not infrequently accompanied by albuminuria. Eckhard[1] confirmed this discovery on dogs and rabbits, and in studying the nerves which influence the activity of the kidneys, came to the following result : In rabbits (but not in dogs) the posterior lobe of the vermiform process of the cerebellum was especially the point, irritation of which, either chemically or mechanically, produced decided hydruria (generally with glycosuria), *without, however, causing a rise of blood-pressure in the aorta.* After division of the splanchnic nerves, injury at this point caused no hydruria, but the excretion of urine remained diminished.—In dogs (but not in rabbits), section of the greater splanchnic nerve on one side caused an increased excretion from the kidney of the same side, which, on irritation of the peripheral extremity of the nerve, gave place to a diminution or an absolute cessation of the excretion. After section of a splanchnic nerve a still further increase of the urinary excretion could be produced by irritation of the fourth ventricle. For the hydruria thus produced there must be, therefore, a nervous channel other than that in the splanchnic nerve (and this is the case both in dogs and rabbits). This channel lies in the spinal cord as far as the seventh cervical vertebra, for a section of the cord above that point abolishes permanently the secretion of urine. Section of the cord below the twelfth vertebra resulted frequently in a permanent slight increase of the urinary excretion. Finally, Peyrani,[1] in numerous experiments on dogs, cats, and rabbits, found that electrical irritation of the cervical sympathetic nerve lasting several hours caused an increase, but section of the same nerve a decided diminution in the excretion both of urine and of urea. According to Claude Bernard, section of the vagus at the cardiac orifice of the stomach causes polyuria; but this statement is as yet without confirmation.

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[1] Beiträge zur Anat. und Physiol. IV. V. and VI.

It is remarkable that, according to Knoll,[2] the urine excreted in increased amount from a kidney after section of the corresponding splanchnic nerve, contains relatively less, but absolutely more, solid constituents, particularly urea, than the urine excreted by the other kidney in the same time.

In what way the above operations on the nervous system produce polyuria, whether it is only by dilatation of the renal arteries, *i. e.*, through vasomotor fibres, or whether it is by a special stimulus to the activity of the kidney, *i. e.*, through specific secretory fibres, must remain undecided, although the latter hypothesis is, according to Eckhard, not improbable in the case of the polyuria produced by irritation of the fourth ventricle.

If we endeavor now to explain by these physiological facts the origin of diabetes insipidus, we can, in the first place, disregard entirely the condition of the *general blood-pressure*. Neither the clinical phenomena of the disease, nor the anatomical changes which have thus far been discovered, afford any ground for the assumption of an abnormally increased arterial pressure, such as would be necessary to account for so considerable and persistent an increase in the amount of urine. Moreover, in those cases in which it would seem probable that a *primary* rise of arterial pressure might exist (*e. g.*, in idiopathic hypertrophy of the left ventricle), nothing of the nature of diabetes has been observed, and in other cases recent experiments on transfusion and on the power of the blood-vessels to adapt themselves to variations in their contents (Worm Mueller[1] and others) make it quite improbable that in a healthy condition of the vascular walls a *permanently* increased arterial pressure can be maintained. It might, to be sure, be assumed that by a continual addition of fluid to the blood the pressure in the vessels might be always increased anew, and thus a persistent polyuria be maintained. This theory is maintained by those who regard the increase of thirst, *i. e.*, the *polydipsia*, as the essential phenomenon of the disease. It is to be noticed, however, that at any rate, in a large majority of cases, the thirst and the greater ingestion of fluids are secondary phenomena dependent upon the increased diuresis, since the latter persists, although in diminished amount, even when the ingestion of water is limited (as has been shown by Neuffer and Neuschler), and since the patients always evacuate more water by the kidneys than healthy persons who drink the same amount, and finally, because their perspiration is very much diminished, all of which is not explained by the assumption of a primary polydipsia, but necessitates the assumption of an abnormal flow of water to the kidneys.

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[1] Comptes rendus. 1870. I. p. 300.

[2] Eckhard's Beiträge zur Anat. und Physiol. 1871. VI. p. 39.

An abnormally *watery constitution of the blood* can also be excluded as a cause of the disease, for nothing justifies such an assumption. On the contrary, we have an analysis by Strauss (see p. 1033), according to which there is a concentration of the blood in diabetes insipidus. Moreover, the assumption is in opposition to the above-mentioned fact that even with the smallest possible ingestion of fluids the kidneys still continue to excrete abnormally large amounts of urine, and, finally, therapeutical results afford no support for the theory that hydræmia is the cause of diabetes insipidus, since the remedies by means of

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[1] Sächsiche acad. Sitzungsberichte. Math.-Phys. Klasse 1873, p. 573.

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which hydræmic conditions are successfully controlled are completely powerless in this disease.

It might with greater probability be supposed that the blood in the disease contains either certain *normal* diuretic substances (urea, salts) in abnormally large amount, or *abnormal* substances of a similar sort, and that the excretion of urine is thus increased in somewhat the same way as in diabetes mellitus the sugar has been supposed to cause the diuresis (see p. 971). But neither of these assumptions can be supported by strong arguments. It is true that in many cases the amount of urea, and in some instances also that of the salts, particularly the sodic chloride, has been found to be increased in the urine, but the increase is by no means in all cases very considerable, nor does it always persist during the whole duration of the disease. Moreover, the diuretic action of urea and of the normal urinary salts is insufficient to explain the great increase in the amount of urine which is observed in diabetes. In order to show the untenable character of the hypothesis it is only necessary to remember that by an abundant meat diet the amount of urea and other solid constituents of the urine can be excessively increased without causing diabetes. The increase in the amount of these constituents can moreover be readily explained as a secondary phenomenon dependent upon the thorough washing out of the tissues by the large amount of water continually passing through them.

As to the production of the disease by an *abnormal* diuretic substance, inosite, which has been found several times in the urine, is the only substance about which the question could arise. But the circumstance that it is not a constant urinary constituent in diabetes insipidus is an argument against the general acceptation of such a theory. A still stronger argument is found in the fact that where it has been found its amount has always been very small, and in fact the investigations of Strauss make it very probable that the occurrence of inosite in the urine is not the cause, but the effect of the increased excretion of urine.

Kuelz[1] also as well as Strauss convinced himself that, when the amount of urine is increased by the ingestion of large amounts of fluid, *inosite* is to be found in small quantities in the urine.

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[1] Sitzungsber. der Marburger Ges. zur Beförderung der Naturw. August, 1875.

We are therefore compelled to seek the ultimate cause of the disease in *disturbances of the above-mentioned nervous channels* which connect the floor of the fourth ventricle and the vermiform process of the cerebellum with the kidneys. Clinical observations and the data of autopsies point decidedly in this direction. In recent times, since greater attention has been paid to diabetes insipidus than formerly, observers have been struck, as in the case of diabetes mellitus (see p. 863), by the frequent association of the disease with nervous disturbances in other parts of the body, and it is especially associated affections in the region of the *medulla oblongata* that have been, in part clinically and in part anatomically, noticed in repeated instances and observed with precision. In view of the above-mentioned results of experimentation, the production of diabetes is in these cases perfectly comprehensible, and the alternation of diabetes insipidus and diabetes mellitus, which has been sometimes observed, is also not surprising. In the same way those cases in which diabetes insipidus occurs in *diseases of the spinal cord* can be, in view of Eckhard's experiments, explained by the assumption that, in the human subject as well as in animals, nerve-fibres, injury to which causes polyuria, have their course for a certain distance in the spinal cord, especially, as it seems, in the lower part. It will be the object of future investigations to determine whether the occurrence or non-occurrence of diabetes insipidus depends upon the location of the disease at a particular height or in a particular column of the spinal cord. Changes in the *sympathetic nervous system*, which, according to Eckhard's and Peyrani's experiments, may also play a part in the production of the disease, must also for the future be more carefully studied than hitherto. Thus far it seems that only in a single case of Dickinson's was the cause of the disease found in a degeneration of the solar plexus (see p. 1033).

Pathology.

Symptoms and Clinical History.

The characteristic symptoms of diabetes insipidus, the augmented urinary excretion and the increased thirst dependent thereon, make their appearance either in the midst of perfect health, or (much more frequently) following after other morbid phenomena which are usually of a nervous character. The nature and duration of these nervous disturbances depend upon the character of the diseases which occasion the diabetes. The disease has been observed to arise in the course of acute and chronic affections of the brain and spinal cord, in connection, therefore, with the greatest variety of symptoms, with derangements of consciousness, of the senses and of speech, with convulsions, paralyses, and disturbances of sensation. In many cases these disturbances had already begun to disappear when the urinary excretion began to increase; in other cases they took on a greater development corresponding to the progress of the malady which occasioned them.

In many cases it is said, to be sure, that no morbid phenomenon preceded the appearance of the increased urinary excretion, especially in cases where it occurred immediately after a striking external exciting cause, as for instance after a wound, a violent emotion, or a great excess in drinking or eating. In many of these cases, however, unimportant nervous phenomena —headache, irritable disposition, wakefulness, etc., were perhaps present, but passed unnoticed, and in the others it may very well be imagined that by the sudden action of external causes a disturbance was produced in the course of the nerves regulating the activity of the kidneys.

The urinary excretion becomes sometimes only very gradually more and more abundant; sometimes it reaches its maximum in the course of a few days. *The amount of urine evacuated in twenty-four hours* is very unequal in different cases, and in the same case at different times. It may vary from a point only slightly above the physiological maximum to ten or twenty times that amount. In most cases it ranges from three to ten litres daily, but cases are reported in which it amounted to over thirty litres, and in one case it rose to forty-three litres (Trousseau), the highest number which has thus far been recorded, leaving out of account those statements in which the calculation is made with uncertain measures, such as pots and pails.

The amount of water evacuated with the urine is in diabetic patients greater than in healthy individuals in the same time and with the same ingestion of fluids (Neuschler, Strauss). This difference, however, is not noticed until a certain time, usually several hours, after the taking of liquid food, for at first the amount of urine is in diabetes not only not greater, but may be even smaller than in health. In a case of diabetes, therefore, the rate of the urinary excretion is not so quickly increased by the ingestion of fluid as in health, but it remains longer at the abnormal height (Falck, Neuschler, Andersohn, Pribram). This delay in the excretion of water is not, as in diabetes mellitus, affected by the simultaneous ingestion of solid food (Neuschler, cf. pp. 895, 954). To explain this peculiarity of the urinary excretion, Falck and others had inferred that there must be a slower *absorption* of water in the intestines. It can, however, be accounted for more naturally and more in accordance with our ideas of the origin of diabetes insipidus (p. 1021), by a *permanent dilatation of the renal capillaries*, in consequence of which the excretion of urine becomes more uniform, whereas in health the ingestion of fluid causes a more sudden dilatation of the renal vessels, and thus a more sudden increase in the amount of urine.

Each *separate evacuation* is often very large, amounting to 500–1000 cubic centimetres, and more, at one time. In other cases the evacuations are smaller, but more frequent, on account of the smaller capacity of the bladder or an irritable condition of the urinary tract, which is not infrequently associated with the disease.

The urine is of exceptionally pale color, when considerably diluted resembling water with a slight greenish tint, and almost always *clear*, at least when freshly evacuated and undecomposed. The peculiar odor of urine is scarcely to be perceived. The reaction is *very faintly acid*, becoming neutral and alkaline more rapidly than usual. The urine then becomes turbid with earthy phosphates and bacteria.

Its specific gravity is always abnormally low.[1] Though, as a rule, varying between 1004 and 1010, it may temporarily, by increase of the solid urinary constituents, approach the lower physiological limit, and at other times sink lower than in any other disease, viz., to 1002, and even to 1001.

The low specific gravity of the urine depends upon the fact that as its amount augments, the increase of the water is proportionately greater than that of all the solid constituents taken together. The latter are, it is true, in most cases absolutely increased, but relatively less than the water. A diminution in their amount occurs only exceptionally and temporarily, never for any great length of time, or during the whole disease, except in consequence of the association of some other malady. The amount of solid constituents in the urine depends chiefly upon the quantity and quality of the ingested food, and these again are (disregarding the external relations of the patient, his occupation and mode of life) dependent upon the character of the affection which occasions the disease, and upon the condition of the digestive organs. A classification of cases, therefore, such as Vogel and others attempted to make, into those with increased and those with normal or even diminished excretion of solid constituents, is, as already stated, not legitimate. (Cf. also p. 1035.)

In the increase of the solid constituents *urea* plays a principal part. The statement of earlier writers that it may diminish in amount, and even absolutely disappear from the urine, must be regarded as an error dependent upon defective methods of investigation. On the contrary, in patients suffering from diabetes, its amount usually exceeds that excreted by healthy persons of the same age. A daily excretion of urea amounting to 40-50 grms. in adult men is not a rare phenomenon, and in two cases I have seen it rise to 70 and 72 grms. respectively. Its dependence upon food has been very strikingly shown by Dickinson in two cases—one, that of a tuberculous girl, eight years of age, of 21 (English) pounds weight, whose daily excretion of urea varied from 6.3 to 30 grms., according as her diet was purely vegetable, mixed, or chiefly animal in its character; whereas the amount normally excreted by a girl of that age amounts to about 6 or 8 grms. In the case of another girl, six years of age, of 20 to 24 pounds weight, and otherwise apparently healthy, who normally should have excreted daily some 5 or 6 grms. of urea, the amount varied, according to the food, from 6.7 to 24 grms.

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[1] *K. B. Hofmann* (Centralblatt für die med. Wissenschaften. 1870. p. 417) describes under the name of diabetes insipidus a case in which 2,500 cubic centimetres of urine, with a specific gravity of 1025, were evacuated in twenty-four hours. This high specific gravity and the circumstance that the urine, after standing several days in an open vessel, still had a strong acid reaction, together with the violent itching of the skin, give rise to the suspicion that this must have been one of those cases of diabetes mellitus in which the urine is capable of holding large quantities of reduced copper in solution, and in which, therefore, *Trommer's* test cannot be applied without special precautions. (See p. 974.)

The increase of the excretion of urea above that which occurs in healthy persons receiving the same amount of nitrogen with their food, is the result of the thorough washing out of the tissues, and of the greater decomposition of albumen which accompanies the passage of an increased amount of fluid through the body (Voit).

Uric acid is generally stated to be greatly diminished and even entirely absent in this disease. It is very probably owing only to the inaccuracy (which is particularly great in very diluted urine) of the method usually employed for its determination (precipitation with hydrochloric acid) that so small amounts have been found.

The same is true of *creatinine*, only three determinations of which are known to me, viz., two by Strauss, of 0.0624 grm. (with 23.425 grms. of urea) and 0.301 grm. (with 15.658 grms. of urea), and one by Pribram of 0.38 grm. (with an abnormally large excretion of urea). In this disease, as in diabetes mellitus (see p. 902), I have myself obtained higher figures corresponding to larger amounts of urea. The quantities, ascertained by repeated determinations, in four cases, which were all those of adult men, varied from 0.544 grm. (with 26.04 grms. urea) to 1.419 grms. (with 70.08 grms. urea).[1]

Hippuric acid is said to have been found by Bouchardat in a case of diabetes insipidus[1] (see Lehmann, Zoochemie. 1858. p. 334).

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[1] Detailed statements will soon appear in Virchow's Archiv.

Sulphuric and *phosphoric acids* are increased for the same reasons as the urea, and vary, as a rule, in the same way. The daily excretion of the former has been found by Pribram, in the case of a man, to be from 3.8 to 5.3 grms., and by Dickinson, in the case of a girl two and one-quarter years old, to be 1.23 grms. The latter I have found in a single determination, in the case of a man, to be excreted at a daily rate of 3.84 grms. (with 54.4 grms. urea); and Dickinson obtained, in the case of a girl eight years old, living on mixed food, a daily amount of 0.58 to 1.3 grms., in the case of the above-mentioned girl two and one-quarter years old, 0.61 grm. (with 9.1 grms. urea), and in the case of a girl three years old, 0.57 grm. (with 23 grms. urea) and 0.6 grm. (with 14 grms. urea).

The excretion of *chlorides* depends upon the nature of the food, but seems to be somewhat increased in consequence of the thorough washing out of the tissues.

Amongst the *bases*, lime (united with phosphoric acid) is said by Dickinson to be particularly increased, and he brings this fact into connection with the nervous origin of the disease, since in many diseases of the nervous system the earthy phosphates, and especially calcic phosphate, are excreted in abnormally large amounts. In the case of the girl eight years old he found in one determination 1.25 grms. of earthy salts and 0.296 grm. of lime alone; in the case of the girl three years old, 0.79 grm. of earthy salts, with 0.176 grm. lime and 0.068 grm. magnesia; lastly, in the case of the girl two and one-quarter years old, 0.248 grm. earthy salts, with 0.039 grm. lime, 0.018 grm. magnesia.

Amongst abnormal constituents *Inosite* has several times been found in the urine in diabetes insipidus, first by Schultzen in two cases, then by Strauss also in two cases, by Gscheidlen (Ebstein) in one case, and by Kuelz in two cases.[2] It is, however, by no means constantly present, for in other cases it has been found wanting by Gallois, Pribram, Gscheidlen (Ebstein), Buerger, Kuelz, van der Heijden, and myself. The amount excreted daily was found by Strauss in one of his patients, a girl ten years old, to be 0.1474 grm.; in the other, a young man twenty-two years of age, to be 1.508 grms. He succeeded in finding in the urine of three healthy men who drank 10 litres of water in 24 and 12 hours respectively, and who consequently had a very abundant urinary excretion, even more inosite than in that of the young man above mentioned, from which he concludes that inosite appears in the urine only because the large amount of water flowing through the body removes it from the tissues, the kidneys, the liver, the lungs, and the muscles before it has undergone its final transformation into carbonic acid and water.

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[1] *K. B. Hofmann* also states that he found hippuric acid in the case designated by him as diabetes insip. (See p. 1024, foot-note.)

[2] In *Mosler's* case also the presence of inosite was inferred from the crystalline form, which is, however, not sufficiently characteristic.

That *sugar* is not found in the urine is self-evident, its presence being inconsistent with the conception of diabetes insipidus. There are, however, certain cases on record in which sugar has appeared temporarily in the urine (Trousseau-Laugier), or in which a diabetes insipidus remained behind after diabetes mellitus, the sugar disappearing from the urine, which continued to be evacuated in abnormally large amounts (Trousseau-Luys, Plagge.[1] Cf. also "Diabetes Mellitus").

Lastly, the earlier writers describe *albumen* as a frequent constituent of the urine in diabetes insipidus—a statement which indicates, however, a confusion of the disease with renal complaints, especially granular atrophy (see "Diagnosis"). In the absence of renal disease, albumen appears very rarely, and only in very small amounts in the urine, perhaps in consequence of the above described (p. 1023) vaso-motor disturbances in the kidneys.

The *thirst* of the patients is in direct proportion to their excretion of urine, rising with the increase of the latter to such a point that the sufferers can scarcely obtain enough fluid to allay it, and in their despair drink even their own urine.

As in diabetes mellitus, so also in this disease, the volume of the excreted urine may exceed that of the ingested fluid, and earlier writers were thus led to speculate upon the possibility of the absorption of water through the skin. But if we add to the ingested fluid the amount of water which is taken with the solid articles of food and that which is formed in the body itself from the hydrogen of the food, the total amount of water always exceeds that which is excreted with the urine, and there is even a surplus for the loss by perspiration or for accumulation in the body.

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[1] Virchow's Archiv. XIII. p. 97.

Appetite and *digestion* are not, as a rule, particularly affected, the disease differing in this respect from diabetes mellitus. Occasionally, in addition to the unquenchable thirst, an insatiable hunger has also been observed (Bernard, Novellis, Trousseau), or a special preference for certain articles of food, or extraordinary longings for indigestible substances, which are to be ascribed to other nervous disturbances, hysteria, etc., rather than to diabetes. In the same way, irregularities of defecation, constipation, or diarrhœa, are, in the majority of cases, connected with the affections which cause the disease rather than with diabetes itself; and the same is true of many other abnormal phenomena which are now and then observed in the functions of the digestive organs, as, for instance, tympanites, nausea and vomiting, heart-burn, attacks of cardialgia, etc.

Among the most interesting phenomena of this sort is to be mentioned the *flow of saliva*, observed by Kuelz, associated for a considerable time with the increased urinary excretion, in the case of a hysterical servant-girl, eighteen years of age. From this patient several hundred (on one occasion 525) cubic centimetres of saliva could be collected in twenty-four hours. To explain this association, Kuelz quotes the above-mentioned experiments of Eckhard on hydruria in dogs and rabbits, in the course of which it was found that salivation sometimes followed puncture of the medulla oblongata. He also alludes to the similar results of Loeb[1] and Gruetzner).[2] It seems, therefore, not unreasonable to attribute the increased formation of urine and saliva in every case to a direct or reflex (*e. g.*, through the uterine nerves) irritation of this nerve-centre.

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[1] Eckhard's Beiträge zur Anat. und Physiol. V. p. 1; and Dissertation. Giessen, 1869. *Kuelz* quotes *Noellner* erroneously, instead of *Loeb. Eckhard* himself had previously made a similar statement (Beitrage. IV. p. 191).

[2] Pflueger's Archiv. VII. p. 552.

The occurrence of diabetes insipidus (polyuria) in hysteria and other nervous diseases explains its not infrequent association with nervous phenomena—*e. g.*, anæsthesia,[1] convulsions, etc.

The skin is generally dry, and has little tendency to perspiration, its supply of water being limited, on account of the abundant stream of fluid which is carried to the kidneys. Consequently, the loss by the so-called insensible *perspiration* is brought considerably below the normal amount, as has been proved by comparative determinations of the weight of the sensible ingesta and egesta, and of the changes in the weight of the body. (Buerger, Cf. p. 928.)

Other affections of the skin, especially furuncles and carbuncles, such as are so common in diabetes mellitus, occur only very rarely in diabetes insipidus, and are to be regarded as accidental complications having no causal connection with the disease. Many cutaneous phenomena (*e. g.*, purpura, œdema) are results of the associated cachexia which may be developed in the course of the affection which occasions the diabetes.

I only know of *one case* (reported by Bourdon) in which diabetes insipidus was developed *after* the appearance of numerous furuncles and one carbuncle. Scrofulous and syphilitic cutaneous eruptions have been often observed in cases where diabetes insipidus has occurred in consequence of diseases of the central nervous system connected with the scrofulous or syphilitic dyscrasia.

On the *other organs* and on the *general health*, diabetes insipidus has, so far as its direct influence is concerned, no effect worth mentioning, if the patients are allowed to drink freely. Those various disturbances, which so frequently arise in consequence of diabetes mellitus, do not occur in diabetes insipidus; or, if they occur, are either to be regarded as accidental complications, or are dependent upon the same fundamental affection as the diabetes itself. The only effect upon the general condition of the patient which can be ascribed to the diabetes insipidus is the *lowering of the temperature*, which is not infrequently observed. It is, however, usually very insignificant (at most a few tenths of a degree centigrade), and is explained by the refrigerant effect of cold beverages ingested in large amounts. (Cf. p. 924.)

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[1] *Oppolzer*, Allgem. Wiener med. Zeitung. No. 38, etc.

A sudden deprivation of ingested fluids may, on the other hand, not only have an injurious effect upon the subjective condition of the patients, who are much distressed by the thirst which torments them, but may also seriously endanger life by the drying of all the tissues which is thus produced.

Considering the frequency of *phthisis*, it cannot be considered surprising that this disease is occasionally observed in a patient suffering from diabetes insipidus; but the frequency of its occurrence in this connection is by no means to be compared with that which is noticed in cases of diabetes mellitus.

The same statement may be made in regard to *disturbances of vision* (especially cataract) which have been occasionally, but upon the whole very rarely, observed. Effusions of blood into the retina have also been sometimes noticed (Galezowski, van der Heijden). Laycock [1] observed in one patient atrophy of the right optic nerve, and in another, who had been formerly syphilitic, a staphyloma posticum.

Disturbances of the *sexual functions* have never been observed as the result of diabetes insipidus.

The course and the duration of diabetes insipidus exhibit great variations, which are generally dependent upon the anatomical changes which occasion the disease. If the latter run through a rapid course, whether favorably or unfavorably, as for instance in traumatic lesions of the skull, the diabetes also lasts only a short time; in some cases, however, it has been known to persist for a considerable time after the healing of an injury to the skull. But in the absence of any fundamental disease which threatens life, diabetes insipidus may have an unlimited duration; in fact, there are few diseases which can afflict a human being for such a length of time as this. Especially are those cases which depend upon a hereditary predisposition, without any recognizable organic disease, remarkable for the length of their duration. The longest duration thus far recorded in a case of this sort is fifty years (R. Willis).

Variations in the course of the disease, *i. e.*, temporary diminution and subsequent increase of the urinary excretion and of the thirst, have often been noticed, and some authors (Maxwell, Bartholin) even observed a complete disappearance of both these symptoms for a longer or shorter time, but without any permanent cure. In other words, the disease assumed an *intermittent* character. A certain influence on the course of the disease, so far as it is not modified by the fundamental lesion, is exerted by *drugs*, the effect of diuretics being injurious, while that of some other medicines is beneficial. The influence of *emotions* is also not infrequently injurious, while the diet has hardly any effect on the course of the disease, which in this respect presents another point of difference from diabetes mellitus.

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[1] Lancet. 1875. Vol. II. No. 7.

Intercurrent febrile diseases produce almost always a diminution of the diabetic phenomena; the thirst becomes more moderate, the amount of urine diminishes, while its specific gravity rises. In a few cases this improvement continues and is permanent after the fever has run its course; in most cases, however, convalescence from the fever is accompanied by a return of the diabetic symptoms.

Cases of intercurrent *varioloid*, with temporary improvement, are reported by Lacombe, Charcot, and Kuelz; of *typhus fever* and some other lighter febrile diseases, by Pribram; of *pleurisy*, in one case followed by permanent cure of the diabetes, by Desgranges; of "*acute rheumatism*," treated with potassic nitrate, and followed by the disappearance of a diabetes of eighteen years' standing, by Roberts (see Dickinson). I myself have observed in the case of a diabetic patient, with a daily urinary excretion of nearly 10,000 cubic centimetres, a diminution in the amount of urine during a *pneumonia* to 1,800 cubic centimetres a day, and a similar diminution occurred in the same man during an *erysipelas*.

A case of *scarlet fever* without any noticeable diminution of the diabetic symptoms has been observed by Dickinson.

Pathological Anatomy.

Very few autopsies of patients who have suffered from diabetes insipidus have been placed on record, because the disease by itself scarcely ever ends fatally, and because the patients are usually not retained during the whole prolonged continuance of the disease in hospitals, where the opportunities for making autopsies are the most favorable; and if they enter the hospitals with an intercurrent disease which ends fatally, the diabetes has usually disappeared.

The most frequent post-mortem appearances are *changes in the brain*, either extending into the medulla oblongata, or located exclusively in this nerve-centre or its immediate neighborhood. *Inflammatory and degenerative conditions of the fourth ventricle* have been several times observed (*e. g.*, by Luys-Trousseau, Martineau, Kien, Lancereaux, Mosler, and Pribram, by the last-named observer associated with caries of the clivus Blumenbachii), as well as *tumors* in the same region or in the cerebellum, namely, *tubercles* and tuberculous meningitis (Roberts, Dickinson), *gliosarcoma* (Mosler); also syphilitic *exostoses* of the cranial roof associated with *gummous tumors of the liver* and *bronchial glands* (Gentilhomme quoted by Lancereaux), and a *fracture of the base of the skull* with contusion of the anterior lobe (Chassaignac).

E. Leudet[1] found in one case (in addition to inflammatory changes in the meninges) the left pedunculus cerebri softened and discolored in its middle portion, and the central part of the floor of the fourth ventricle colored pale yellow. In another case the pituitary gland was converted into a fibrous tumor.

Carcinoma of the pineal gland was observed by Massot in the case of a workman nineteen years old.

The *kidneys* are often described in the earlier reports as affected with granular or cystic degeneration; but these cases, which, during life, were characterized by albuminuria, are not, as above repeatedly remarked, to be regarded as diabetes insipidus. In some other cases the kidneys have been found simply enlarged and hyperæmic, which may very likely depend upon their greater activity during life. In one case, where there was no change in the gross appearance of the kidneys, the microscope showed the urinary tubules to be greatly dilated—some deprived of their epithelium, and others filled with epithelial cells in a state of fatty degeneration (Neuffer).

Among organic diseases observed in other parts of the body are to be mentioned *lobular pneumonia* (Neuffer) *and cavities in the lungs* (Luys-Trousseau); *a fibrous tumor between the uterus and rectum*, which had compressed the intestine, together with *enlargement of the mesenteric glands* (Haughton[1]); and lastly, *cancer of the liver* and of the abdominal lymphatic glands, with *degeneration of the solar plexus* (Dickinson).

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[1] Clinique méd. de l'Hotel Dieu de Rouen. Paris, 1874. p. 322.

Two determinations of the composition of the *blood* have been made by Strauss. The blood was taken from a young man nineteen years of age, suffering from diabetes of ten years' standing, but otherwise in good health. Its composition was as follows:

	1st Observation.	2d Observation.
Water	77.79	77.937
Solid constituents	22.21	22.063
	100.00	100.000

The solid constituents of the second specimen of blood contained: fibrin, 0.467; hæmoglobin, 11.72; other albuminoid substances, 7.441; extractive substances, 1.301; ashes, 1.134 per cent. The serum of the blood contained, in 100 parts, 88.712 water and 11.288 solid constituents, the latter consisting of albumen, 9.062; extractive substances, 1.012; and ashes, 1.214.

The blood showed, therefore, in comparison with normal blood, an increase of the solid constituents.

Diagnosis.

It has been already pointed out in the introduction that every abnormal increase of the urinary excretion is not to be regarded as diabetes insipidus. The fact of an actual increase in the amount of urine being established, the diagnosis depends mainly upon the exclusion of the conditions also there enumerated. In this connection it is perhaps not superfluous to remark that patients, who from any cause are obliged to pass their water frequently, usually state that they evacuate an abnormally large amount of urine. Their assertions must therefore be tested by measurement of the actual amount voided in twenty-four hours.

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[1] Dublin Quarterly Journal. 1863. Nov. p. 323.

Moreover, since the daily excretion of urine, even under physiological conditions, varies within pretty wide limits, it is impossible to establish any fixed point above which the amount of urine is to be regarded as abnormal. In cases where the amount of the daily urinary excretion keeps near the upper limit of the normal quantity, it is necessary, before assuming the existence of any disease, to take into account all the conditions and circumstances of the patient, especially everything which is known to have an influence on the amount of urine, and also, if possible, to ascertain the quantity of urine which the patient formerly evacuated; and even then it will often be doubtful whether a pathological condition exists or not. There is also some room for individual preferences in deciding whether the case is one of temporary or more persistent increase of diuresis, for only in the latter case is it customary to speak of a diabetes. An increase in the amount of urine which lasts only a day or a few days is not usually so designated.

Of chronic conditions which may be mistaken for diabetes insipidus are to be considered: first, *diabetes mellitus*, and secondly, various *renal diseases.* The former is readily excluded by the low specific gravity of the urine, and by the negative result of the sugar-test. Amongst renal diseases may be mentioned especially *contracted kidney*, *amyloid degeneration*, *pyelitis*, and *hydronephrosis*, as maladies which are characterized by a permanently or intermittently increased excretion of a pale urine of abnormally low specific gravity, and which were, therefore, formerly confounded with diabetes insipidus. The most important means of differentiating in such cases is testing for albumen, whose presence always excites a suspicion of one of the above-mentioned diseases, and always necessitates great caution in diagnosticating diabetes. The absence of albumen by no means excludes the above diseases with certainty. Repeated examinations of the urine, extending over a considerable time, and the consideration of other circumstances—for an account of which the reader is referred to the special description of renal diseases (see Vol. XV.)—are, then, necessary to establish the diagnosis, which, after all, may frequently remain doubtful. As reasons for diagnosticating a diabetes insipidus in such doubtful cases may be regarded: a very low specific gravity of the urine, viz., below 1004–1005, and great thirst, especially if both these symptoms persist for any considerable length of time, for this combination of symptoms is in no other disease so strongly pronounced

Results and Prognosis.

Permanent recovery from this disease is rare, but death, in uncomplicated cases, is still more rare. In the literature of the subject there is only one such case (reported by Neuffer), in which death occurred after the disease had lasted barely four months, without any other morbid condition to which death could be attributed, the fatal result being preceded by gradually increasing weakness and diminution of the urinary excretion and thirst. Usually the patients die of an intercurrent disease, or of the malady in the course of which the diabetes has arisen, and which is to be regarded as its cause (affections of the brain or spinal cord).

In the cases which have been reported as ending in recovery the disease had generally lasted only a short time, *i. e.*, not more than a few months; in some few instances it had had a duration of several (3–4) years. As above mentioned, recovery has been sometimes brought about by an intercurrent disease. In one instance the diabetes, which had occurred during pregnancy, disappeared two days after confinement (Bennet); in another case, on the contrary, the disease, after lasting several years, disappeared with the commencement of pregnancy; while in several other cases pregnancy had no effect whatever. (Matthews-Duncan.[1])

The *prognosis*, so far as life is concerned, is therefore not unfavorable (for it is almost never the diabetes insipidus which occasions death); on the other hand it is, in respect to recovery, very doubtful.

Since R. Willis called attention to the increase of urea in the urine, and proposed the name of azoturia for this condition, and especially since J. Vogel insisted upon the distinction between hydruria and diabetes insipidus on account of the increase of the solid constituents which occurs only in the latter, many observers, following the example of the last-named writer, have given a variable prognosis according as the amount of solid constituents in the urine has been found to be abnormally increased or not. In diabetes insipidus, in Vogel's sense of the word, danger was supposed to arise from the impoverishment of the body in respect to its solid constituents, the excretion of these substances being in excess of their ingestion. I have already stated above (p. 1024) that, except in the case of intercurrent disturbances, the solid constituents, and especially the urea, are almost always excreted in abnormally large amount, and that a chronic hydruria, in Vogel's sense of the word, does not exist as an independent malady. Whether the excretion of solid constituents is much or little in excess of the normal amount depends upon the quantity ingested, *i. e.*, upon the appetite of the patient. As long as the patients retain their appetite and can satisfy their thirst, they are in no danger, and there is, therefore, fortunately no need, for the sake either of diagnosis or of prognosis, of a minute and lengthy determination of the solid constituents of the urine.[1]

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[1] Obstetrical Journal of Great Britain and Ireland. 1874. July. p. 220.

Treatment.

There are no special *prophylactic* measures for diabetes insipidus.

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[1] *Vogel* states, it is true, that the percentage of solid constituents in the urine can be ascertained, at least approximately, by the well-known method of multiplying the two last figures of the specific gravity determined to three places of decimals by 0.2 (more accurately by 0.233, according to *Haeser*); but this calculation gives very uncertain results in the case of urine so diluted as that which is evacuated in this disease. *Neubauer's* analytic vouchers for the method (see *Neubauer* and *Vogel*, Anleitung zur Analyse des Harns. 1872. p. 239) have reference only to urine of a specific gravity above 1.011, and the determination is, moreover, made carefully to four places of decimals.

Equally inaccurate results are obtained by means of the formula given by *Traube* in his lectures (see Schlesinger's Dissertation) for finding the "reduced specific gravity," *i. e.*, the specific gravity which the urine would have if its solid constituents were dissolved in the normal amount of urine. This formula is: $S-1=\frac{V_1}{V}(S_1-1)$, in which S denotes the required reduced specific gravity, S_1 the true specific gravity of the diabetic urine, V_1 its volume, and V the normal volume (1,700 c.c).

The *real treatment* must, in those cases in which the affection occasioning the disease is known and accessible to therapeutic measures, be of course, first of all, directed to this malady, and may then have good results. Thus, in syphilitic affections of the skull and brain, a mercurial treatment has been found useful, in diseases of the spinal cord a certain success may be expected from a treatment directed to these complaints, and in hysteria from anti-hysterical remedies and methods. A treatment of this sort directed to the cause of the disease is, whenever possible, all the more strongly indicated from the fact that of all the other remedies recommended in this complaint not one is absolutely certain in its action, and those which are most efficacious are not free from disagreeable secondary effects, and are particularly apt to spoil the appetite of the patients.

Since diabetes insipidus is rather a troublesome than a dangerous complaint, it is advisable in the lighter cases to avoid the administration of drugs, and to recommend to the patients only a *careful attention to the skin*, warm clothing, warm baths, frictions, etc., in order to divert a portion of the stream of fluid from the kidneys to the skin. In severer cases the patients may be advised, in addition to this, to quench the distressing thirst not by excessive drinking, but by bits of ice and acidulous fluids, and of the many much extolled remedies the most harmless may first be tried. Especially to be recommended as possessing this character are *Valerian root*, which, according to Trousseau, is sometimes useful in doses of several (up to twelve) grammes daily, and the *constant current* on the spinal column and the renal region, which has also been employed successfully (Kuelz). Hanfield Jones also found *Valerian root* in his case[1] efficacious in diminishing the amount of urine, while the convulsions seemed to become more violent under its influence.

Opium and its alkaloids have often, though only temporarily, diminished the thirst and the amount of urine; but, owing to their tendency to disturb the digestion, they should be employed only in cases of absolute necessity. Other narcotics also, *e. g.*, belladonna, potassic bromide, as well as astringent remedies of all sorts, as tannin, lead acetate, ergot, have been recommended; lastly, a large number of purely empirical remedies which are not worth the trouble of enumerating. The latest remedy, which has proved useful in one case, is *jaborandi* (Laycock[1]); its favorable action may perhaps depend upon its promoting the secretion of the sweat and the saliva.

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[1] Med. Times and Gazette. 1875. No. 1328.

Sidney Ringer[2] found *ergotin* efficacious, but *jaborandi* of no use.

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[1] Lancet. 1875. Vol. II. No. 7.

[2] British Med. Journal. 1875. No. 782.

TRANSLATOR'S NOTE.

Since the pages on the treatment of acute rheumarthritis were written, two new remedies for this disease have come into use, viz., salicylic acid with its salts, and salicin, the active principle of willow-bark. The pressure of other business having prevented Dr. Senator from contributing the needful supplement on this important subject, the following brief remarks are added, at his desire, by the translator.

Kolbe's discovery of a cheap and easy method of preparing salicylic acid in large quantities (by the action of carbon dioxide on phenol), and its employment by Prof. Thiersch for antiseptic dressings, drew attention to this compound in the year 1874. The internal administration of the acid and its salts (more especially sodium salicylate) speedily showed them to be endowed with very marked antipyretic properties. Given in large doses to patients suffering from enteric fever, phthisis, erysipelas, and other febrile affections, they were found almost invariably to cause a considerable fall of temperature; it was soon perceived, however, by impartial observers, that this fall of temperature was not attended by any simultaneous modification of the local morbid process, by any constant improvement in the other symptoms of the disease, by an appreciable lessening of its mortality. To this unfavorable conclusion, however, there was one signal exception. Administered in acute rheumarthritis, salicylic acid and the salicylates were found not merely to reduce the heat of the body, but to exert a beneficial influence (which, owing to our ignorance of its intimate nature, we may call "specific") on the joint-mischief and the course of the disease as a whole.

The following is a summary of the more important points which have been ascertained, up to the present time, concerning the action of salicylic acid and sodium salicylate in rheumarthritis.

1. There seems to be no essential difference between the acid and the salt. The latter is the most soluble of the two; hence, it is more quickly absorbed into the blood, and more rapid in its action. It appears to be somewhat less powerful, in equal doses, than the uncombined acid.

2. From 10 to 20 grains of salicylic acid or a salicylate should be given every hour or every two hours till relief is obtained. This usually ensues in from 12 to 36 hours after the administration of the remedy has been begun. The latter should then be omitted, or given at less frequent intervals. Relapses ought to be treated like the original attack.

3. In a vast majority of cases the fever and the pain and swelling of the joints abate within a period of from 24 to 48 hours. This is the chief, as it is the first, effect of the remedy. In some cases the disease is altogether arrested; in others, its duration is much shortened.

4. Complications (peri- and endocarditis, pleurisy, pneumonia, etc.), when present, are not influenced by the drug, neither are they prevented from occurring, save indirectly, owing to the arrest of the disease.

5. When acute rheumarthritis is attended by hyperpyrexia with severe head-symptoms, the salicylic treatment cannot be relied upon to avert the fatal issue. We must continue, in these comparatively rare cases, to put our trust in the methodized employment of cold baths.

6. In a considerable proportion of cases, salicylic acid and its salts give rise to disagreeable symptoms, such as vertigo, headache, tinnitus aurium, and deafness, nausea and vomiting after every dose, profuse sweating, great weakness, and occasionally a peculiar eruption on the skin. More rarely, the symptoms assume a dangerous complexion, violent delirium, albuminuria, great prostration, with pallid skin and feeble pulse, ushering in fatal collapse. Such accidents have been ascribed to contamination of the remedy with phenol, owing to some mishap during its manufacture. They have undoubtedly been observed, however, after the administration of perfectly pure samples of the drug.

Pursuing an altogether independent train of thought, and ignorant of what had been done in Germany with salicylic acid, Dr. Maclagan (in November, 1874), was led to try salicin in a case of acute rheumarthritis. The result surpassed his anticipations, and in March, 1876, he published a series of eight cases treated with this medicament. The following is a short abstract of the principal conclusions at which he arrived, and which have been, in the main, substantiated by other observers.

1. The benefit to be expected from salicin is greater in proportion as the malady is more acute.

2. In acute cases, its good effects are generally apparent in 24, always within 48 hours of its administration in sufficient doses.

3. When given at the commencement of an attack, it appears *sometimes* to arrest the course of the malady as effectually as quinine arrests ague, or ipecacuanha dysentery.

4. Relief of pain is always one of the earliest effects produced. In acute cases, relief of pain and fall of temperature are generally simultaneous. In subacute cases the pain may be decidedly relieved before the temperature begins to fall; this is especially noticeable when, as often occurs in persons of nervous temperament, the pain is out of proportion to the fever.

5. To be of any use, salicin must be given in large doses, *sc.* 10 to 30 grains every two, three, or four hours, till relief is obtained; 15 grains every three hours is a medium dose for an adult male.

The two methods of treating rheumarthritis—with salicylic acid and its salts, and with salicin—have recently been brought into connection by Dr. Senator. (*Berlin. klin. Wochenschrift.* 1877. Nos. 14 and 15.)

It has long been known that salicin, when acted upon by ferments such as ptyalin or emulsin, splits up into saligenin and glucose, saligenin being readily oxidizable into salicylic acid. Ferments capable of effecting the former of these changes abound in the living organism, and Senator concludes that the dissociation of salicin begins as soon as the glucoside enters the stomach. The resulting saligenin is believed to undergo oxidation in the blood, salicylic acid being thus generated in close proximity to the tissue-elements. To show the rapidity with which the conversion of salicin into salicylic acid takes place in the system, Senator relates the following experiment: He swallowed thirty grains of salicin in powder; from fifteen to twenty minutes later, his urine gave a violent reaction with ferric chloride, showing that it already contained salicylic or salicyluric acid.

It is accordingly affirmed by Senator that the action of salicin is fundamentally the same as that of salicylic acid. As an antipyretic it is less powerful, but it appears to extend its action over a longer period of time. In one very important respect it is superior to salicylic acid and the salicylates, especially for administration in a disease like rheumarthritis, which is so often attended by serious cardiac troubles; it does not give rise to any of the disagreeable or even dangerous accidents which are far from uncommon after the latter group of remedies.

Senator's own experience leads him to think very highly of salicin in the treatment of acute rheumarthritis. He has also prescribed it, with excellent effect, in atonic gout and other chronic articular affections; it exerts a very favorable influence on the stiff and painful condition of the joints.

E. Buchanan Baxter.

END OF VOLUME XVI.

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